Does surface neuromuscular electrical stimulation (sNMES) to the upper limb following acute stroke improve outcome?

Dr. Catherine Jayne Church
School of Clinical Medical Sciences and School of Population & Health Sciences
University of Newcastle upon Tyne
Supervisors: Dr. Helen Rodgers and Dr. Christopher Price
MD (full-time) registered 1/11/01

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by

Catherine Church

A thesis submitted for the degree of

MD

University of Newcastle-upon-Tyne

2006

Date: 31st March 2006

Abstract

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Introduction: Upper limb impairment affects 85% of stroke patients, half of whom still experience problems three months later[1-3]. The literature is unclear about the effectiveness of upper limb rehabilitation strategies, and there is a need to identify interventions that will improve upper limb function and reduce the incidence of shoulder pain. Surface neuromuscular electrical stimulation (sNMES) has been proposed as a safe method of improving outcome after stroke but further research is needed to evaluate the effect of this treatment on upper limb recovery and pain[4, 5].

Aims: We have undertaken a randomised controlled trial to evaluate a programme of upper limb sNMES following acute stroke.

Methods: Patients admitted within 10 days of acute stroke were assessed against the following eligibility criteria: new upper limb impairment (motor and/or sensory and/or neglect); medically stable; no cognitive/language impairments or previous upper limb problem likely to influence assessments; no contraindication to sNMES. Participants were randomised via an independent telephone randomisation service to receive a 4-week programme of upper limb sNMES (1 hour three times daily) or placebo in addition to stroke unit care. The active stimulator produced a shoulder shrug. Outcome measures were undertaken by a researcher who was blinded to the randomisation group. The primary outcome measure was the Action Research Arm Test (ARAT)[6, 7] 3 months after stroke. Secondary outcome measures included upper limb pain, disability and health status. One hundred and sixty eight subjects were required for 80% power to detect a clinically significant difference in ARAT (8 points)[6, 7].

Results: There were 176 study participants. The groups were well matched at baseline. There was no difference in arm function between groups in terms of the primary outcome measure. The median ARAT[6, 7] score at 3 months was 50.0 in the intervention group (n=79) and 55.5 in the control group (n=74) (p=0.068). There were however significant differences in outcomes in favour of the control group when using other measures to assess arm function (the grasp and gross subsections of the ARAT[6, 7], and the Frenchay Arm Test (FAT)[8]). There was also a significant difference in favour of the control group when

assessing impairment using the Arm subsection of the Motricity Index[9]. There were no statistically significant differences between the groups at 3 months in terms of prevalence of upper limb pain, disability and global health status. No significant differences were seen between the groups at 4 weeks in any of the outcome measures.

Secondary analysis revealed statistically significant differences in favour of the control group in those with more severe initial functional impairment.

Subjects received 70% of intended stimulation or placebo with no significant difference between groups.

Conclusions: A 4-week programme of sNMES to the shoulder does not improve functional outcome following acute stroke and may worsen arm function in certain stroke patients. 'Routine' use of sNMES to the proximal upper limb after acute stroke cannot be recommended.

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Acknowledgments

The author wishes to thank:

The study participants, and all of the ward staff and therapists within Northumbria Healthcare NHS Trust who provided assistance on the project.

The Project Team

- My supervisors, Dr Helen Rodgers and Dr Christopher Price, for their help and continued support.
- Mrs Ruth Wood for her work on the project database.
- Mrs Dawn Winpenny and Mrs Deborah Jones for providing secretarial and administrative support.
- Dr Stuart Huntley, Dr Richard Curless and Dr David Pandyan for their encouragement and support.
- Mrs Judith Murdy and Mrs Ailsa Scott, Research Nurses, for their hard work on the project.

Funding

My thanks go to:

Northumbria Healthcare NHS Trust

Remedi

Department of Medical Physics and Biomedical Engineering, Salisbury District Hospital for providing the electrical stimulators.

University of Newcastle Ladies Golf Club for their generous donation.

Also to Dr Tony Rudd and Dr Elaine McColl, my MD examiners, for their helpful comments regarding this thesis.

Publications and Presentations

Abstracts

Church C, Price CI, Huntley S, Curless R, Pandyan AD, Rodgers H
Does surface neuromuscular electrical stimulation to the shoulder following acute stroke improve outcome?
Stroke 2005; 36: 422

Platform presentations

Church C, Price CI, Pandyan AD, Huntley S, Curless R, Rodgers H
Does surface neuromuscular electrical stimulation to the shoulder following acute stroke improve outcome?
Northern BGS meeting
Newcastle upon Tyne, UK, March 2005

Church C, Price CI, Huntley S, Curless R, Pandyan AD, Rodgers H
Does surface neuromuscular electrical stimulation to the shoulder following acute stroke improve outcome?
International Stroke Conference
New Orleans, US, February 2005

Church C, Price CI, Huntley S, Curless R, Pandyan AD, Rodgers H
A randomised controlled trial to evaluate surface neuromuscular electrical stimulation to the shoulder following acute stroke.
British Association of Stroke Physicians Annual Scientific Meeting
Newcastle upon Tyne, UK, January 2005

Pandyan AD, Price CI, Church C, Huntley S, Curless R, Rodgers H
A randomised controlled trial to evaluate surface neuromuscular electrical stimulation to the shoulder following acute stroke.
International Functional Electrical Stimulation Society Annual Conference
Bournemouth, UK, September 2004

Paper

Church C, Price C, Pandyan D, Huntley S, Curless R, Rodgers H

A randomised controlled trial to evaluate surface neuromuscular electrical stimulation to the shoulder following acute stroke.

Submitted December 2005

List of Abbreviations

ADLs	Activities of Daily Living
ARAT	Action Research Arm Test
BT	Botulinum toxin
CC	Dr. Cath Church, Research Fellow
DT	Drawing Test
EADLs	Extended Activities of Daily Living
EMG	Electromyography
EMG-stim	EMG triggered electrical stimulation
ES	Electrical stimulation
F-M	Fugl-Meyer
FAT	Frenchay Arm Test
FAM	Functional Assessment Measure
FES	Functional electrical stimulation
FIM	Functional Independence Measure
fMRI	Functional Magnetic Resonance Imaging
HR	Dr. Helen Rodgers, Lead Investigator
IQR	Inter quartile range
LACS	Lacunar stroke
MAS	Motor Assessment Scale
MMAS	Modified Motor Assessment Scale
MRC	Medical Research Council
NMES	Neuromuscular electrical stimulation
NIHSS	National Institute of Health Stroke Scale
NTGH	North Tyneside General Hospital
OHS	Oxford Handicap Scale
QOL	Quality of Life
PACS	Partial anterior circulation stroke
PET	Positron emission tomography
PFST	Positional feedback electrical stimulation
pNMES	Percutaneous neuromuscular electrical stimulation
POCS	Posterior circulation stroke
PROM	Passive range of movement
RCT	Randomised controlled trial
ROM	Range of movement
RUE/MAL	Reduced upper extremity motor activity log questionnaire

SEPs	Somatosensory Evoked Potentials
SLROM	Shoulder lateral range of motion
sNMES	Surface neuromuscular electrical stimulation
TACS	Total anterior circulation stroke
TENS	Transcutaneous electrical nerve stimulation
TES	Therapeutic electrical stimulation
UEFT	Upper Extremity Functioning Test
VAS	Visual Analogue Scale
WGH	Wansbeck General Hospital
WHO	World Health Organisation

Chapter 1 Introduction

1.1 Epidemiology

Stroke is the third largest cause of death in the United Kingdom and is the commonest cause of severe adult disability[10]. Each year, 110 000 people in England and Wales have their first stroke, and 30 000 people have a recurrent stroke[11, 12]. The prevalence of stroke and stroke-related disability rise with age[13, 14] and the consequences to individuals and their families can be devastating[15, 16]. Stroke patients are major users of NHS and social services resources[17]. Stroke prevention and treatment is a national priority as addressed in the National Service Framework for Older People and the National Service Framework for Coronary Heart Disease[11, 18].

1.2 Recovery after stroke

Movement depends upon multiple regions of the central nervous system, including the primary, supplementary and cingulate motor cortices, and premotor cortex. The subcortical and brainstem regions also play an important part. The sensorimotor regions of the central nervous system demonstrate activity-dependent plasticity which is seen both in normal learning and in response to cerebral injury[19]. Plasticity, or cortical reorganisation, is defined as 'any enduring change in the cortical properties, either morphological or functional'[20].

Reorganisation of the affected sensorimotor cortex occurs by a variety of mechanisms and is a major contributor to recovery after stroke. The specific neurological mechanisms that mediate the neuromuscular recovery process after a stroke are not completely understood. Substantial changes in neuronal circuits are seen adjacent or connected to the infarct, including dendritic and axonal sprouting, and stem cell responses. Dendritic sprouts also grow with normal learning and in both the contralesional and ipsilesional cortex in association with limb use in rodents[21, 22]. Axonal sprouting occurs in response to a specific signal produced by ischaemic brain lesions. This sprouting after stroke occurs in both local and long distance connections and produces new projection patterns in the brain. It appears to play a role in functional recovery[23]. The stem cell response to cortical ischaemia results in proliferation, migration, and differentiation of new neurons into areas of damage adjacent to the stroke. Unlike axonal sprouting, there is no correlation between the post-stroke stem

cell response and functional outcome[19]. Through these processes, adjacent brain remodels after stroke and creates entirely new systems of connections.

Motor learning and re-learning occurs as a direct result of experience or practice i.e. activity-dependent plasticity. This occurs within cortical, subcortical and spinal levels of the neuroaxis. Repetitive exercise enhances or guides neuroplastic recovery processes after brain injury. The learning process is based on the constant plasticity of the nervous system, and requires afferent input to the central nervous system. The 'sensorimotor integration theory' postulates that the somatosensory cortex interacts extensively with the motor cortex during motor re-learning[24]. Neural mechanisms in the cerebral cortex association areas integrate sensory and motor functions during the perception/action of executing voluntary purposeful movement. Animal studies have shown an enlargement of the motor cortical representation in monkeys subjected to rehabilitative training after experimental stroke in the motor cortex[25]. In addition, positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) have been used to look at brain plasticity in relation to normal learning, and also at the reorganisation of functional representations in relation to recovery from cerebral injury e.g. stroke. The overuse or disuse of particular inputs has been shown to lead to an increase or decrease, respectively, of the corresponding cortical representations.

1.3 The upper limb after stroke

Patients with hemiplegia often feel that therapy has concentrated upon mobility and discharge planning and that not enough attention has been paid to improving arm function[26]. Upper limb impairment affects 85% of stroke patients, of whom 55-75% still experience problems 3-6 months later[1-3]. In contrast, around 80% of survivors will be able to walk again[27, 28]. Poor upper limb function is an important adverse prognostic indicator for subjective well being[29] and is also associated with pain, particularly at the shoulder, which is reported by approximately 50-70% of patients at least once during the first six months after stroke[30, 31]. Identifying effective programmes to improve upper limb function and reduce the frequency of shoulder pain remains a challenge for stroke rehabilitation services.

1.3.1. Shoulder pain

Shoulder pain is a common complication of stroke and can result in limited functional use of the affected limb, compromised recovery, and delayed discharge from hospital. It has been shown to be a predictor of poor recovery of upper limb function following stroke[32]. The frequency of shoulder pain following stroke is reported to vary between 5 and 84%[33]. This variation probably reflects differences in study design and the difficulties in measuring and quantifying pain.

The causes of shoulder pain following stroke are thought to be multifactorial. It appears that changes in anatomy which occur both in the flaccid and spastic stages following stroke may contribute to pain through different mechanisms[33]. In flaccid paralysis of the shoulder, weakness of the shoulder girdle muscles and gravitational pull tend to produce inferior subluxation[34]. Also, weakness in the muscles effecting scapular and humeral rotation during elevation results in failure of the mechanisms which normally prevent impingement, increasing the risk of rotator cuff damage[35]. The weight of the unsupported arm may also cause traction damage to various nerves[36]. With the development of spasticity, supraspinatus tends to reduce inferior subluxation, although this may not occur if there has been permanent stretching or damage to the rotator cuff[35]. Soft tissue damage from improper handling of the affected upper limb may contribute further to shoulder pain[37].

The incidence of pain is related to severity of weakness, and the likelihood of developing it increases over time. Abnormal upper limb sensation is also strongly predictive of the development of shoulder pain[38]. The association of subluxation and shoulder pain is complex and this is thought to be due to variations in measuring both subluxation and pain, and a failure to identify other causes of shoulder pain in study populations. It has been very difficult to identify cause and effect[39].

The management of shoulder pain following stroke is often difficult because of the diverse and multifactorial aetiology of hemiplegic shoulder pain[33, 38, 40]. The use of slings and supports remains controversial[33, 39]. Early passive movement has been shown to be beneficial in the prevention of immobility and soft tissue contracture[41]. The evidence for the use of ES in treating and preventing hemiplegic shoulder pain will be discussed below. Oral analgesia has been shown to be of some benefit, as has the use of local injections e.g. nerve blocks, botulinum toxin, although the use of local steroid injections is not recommended[33].

1.4 Upper limb rehabilitation

The World Health Organisation's International Classification of Impairment, Disability and Handicaps (WHO ICIDH) was published in 1980. This model of illness has 4 levels: pathology, impairment, disability and handicap[42]. Pathology refers to the abnormal processes occurring within an organ or organ system, impairments are the direct consequences of the underlying pathology (i.e. symptoms and signs), disability is the functional consequence of any impairment, and handicap is the social consequence of the disease.

The above model has been updated by the World Health Organisation's International Classification of Functioning (WHO ICF)[43] published in 2001. The ICF describes illness in terms of impairments of body functions, impairments of body activities, activity limitations and participation restriction, environmental factors, and other contextual information. Both this model and the ICIDH provide frameworks within which the many aspects of ill health can be described. These models have been used to define rehabilitation. For example, Wade described rehabilitation as "a problem-solving and educational process aimed at reducing the disability and handicap experienced by someone as a result of a disease, always within the limitations imposed both by available resources and by the underlying disease"[44].

Epidemiological studies have shown that early physiotherapy and mobilisation after stroke is beneficial[45, 46]. Three systematic reviews[45, 47, 48] suggested that early intensive stroke rehabilitation may be associated with enhanced and faster improvement of activities after stroke, and the intensity of repetitive training has been shown to facilitate motor recovery[49]. There has, however, been some concern regarding early overuse after cerebral ischaemia in rodents, raised by experimental models[50]. There is also animal data to suggest that, although early intensive intervention after ischaemia can improve functional outcome, it is accompanied by increased brain damage[51]. This is thought to be due to increased glutamate release by damaged cells, but the relevance of these findings in humans is not known. In addition to the evidence surrounding greater intensity, repetitive training in upper limb rehabilitation, it is also clear that learning a skill requires feedback. Studies suggest that task-orientated or task-specific practice is best for skills learning[49, 52].

There are many interventions that aim to improve upper limb function following stroke but the literature is unclear about the effectiveness of many of them. Such interventions include intensive therapy programmes[48, 49, 53-56], home based exercise programmes[57, 58], strategies to overcome non-use of the hemiplegic arm[52, 59, 60], electromyographic biofeedback[61], and

electrical stimulation[5, 62]. Intensive therapy programmes were shown to be beneficial in a study by Kwakkel[49], but not in studies by Lincoln[54] or Rodgers[55]. Reviews of the literature have concluded that such programmes may be effective following stroke despite the fact that firm evidence of this is lacking[56]. Home-based exercise programmes have been shown to be feasible but studies have not shown consistent benefits in terms of functional recovery[57, 58]. Strategies to overcome non-use of the affected upper limb, e.g. constraint therapy, have been shown to be of benefit in improving function, but they were small, single-centre studies and therefore prone to false-positive results[63]. Also, in the study by van der Lee[52], the functional improvement was judged only to be of clinical benefit in those with sensory loss or neglect, and in Dromerick's study[59], the follow-up period was only 2 weeks and the improvement seen in function did not clearly translate into a benefit on ADLs. A 6-week programme of electromyographic biofeedback has been shown to improve upper limb function following stroke but this was not sustained 6 weeks after treatment[61]. The evidence of the effect of ES on recovery following stroke will be discussed in more detail in Section 1.6.

As the majority of functional recovery occurs within the first six months after stroke and is most rapid within the first few weeks - if concepts of neuroplasticity are accepted[64] - then the maximum opportunity to improve recovery is offered by early intervention. This may improve the rate of recovery even if the overall level achieved is no greater[48, 56]. Most studies that have assessed the clinical efficacy of these interventions have recruited patients several weeks or months after stroke.

Another explanation for the lack of effectiveness of upper limb rehabilitation techniques might be the failure to target interventions at those who are likely to gain most benefit. Upper limb impairment following stroke is due to a variety of motor and sensory deficits and it therefore seems unlikely that one rehabilitation approach will be suitable for all. Studies have tended to use one intervention in a mixed impairment population, so potentially diluting any effect, or use a complex intervention (such as intensive therapy), which has not been well defined and is difficult to generalise.

Attempts have been made to identify clinical features that will predict upper limb recovery so that interventions can be targeted appropriately. For example, studies have shown that the severity of initial upper limb motor impairment is a predictor of upper limb recovery[65] and, in addition, early proximal muscle activity is believed to indicate a good prognosis[66]. Trials can therefore be designed to identify individuals who may be more or less likely to benefit from the intervention under examination.

It has also been shown that shoulder pain is correlated with initial upper limb motor impairment and is as powerful for predicting motor recovery at 6 months as initial motor score[67]. The relationship is complex as upper limb weakness may also be a risk factor for both poor recovery and shoulder pain but the interaction between them is unclear.

1.5 Measurement of outcome of upper limb rehabilitation

There are a variety of scales available for measuring outcomes of upper limb rehabilitation. Measurement is 'the use of a standard to quantify an observation' and should be distinguished from assessment which is 'the process of interpreting the measurement'[44]. The British Society of Rehabilitation Medicine recognises that no single tool can be used in outcome measurement but, in selecting scales, they state that it is important to take into consideration what is to be measured (e.g. function, disability), in what type of problem (e.g. neurological, musculoskeletal), and in which particular setting (e.g. hospital, community)[68]. It is also vital to choose scales that are well validated and reliable. A measurement is valid if it accurately describes the underlying phenomenon or disease, and reliable if the measurement error (i.e. the intra- and inter-observer variability) is minimal[69]. Outcome measures chosen should be relevant to the rehabilitation intervention and sensitive i.e. able to differentiate within a patient group and identify meaningful differences in their abilities[19]. They should also be simple to use, give results that are easily understood by others[44] and, if possible, widely used in the clinical setting.

Measures of 'arm function' usually assess motor control, manual dexterity or performance in a series of tasks involving both proximal and distal abilities. Many of the tests used to assess arm function are in fact measures of impairment. Others relate to specific arm abilities (i.e. they look at focal disability) or general abilities that depend on use of the upper limb.

The outcome measures discussed in further detail below are those most commonly used in studies of sNMES to the upper limb. Measures used in this study (indicated by an asterisk) assessed a variety of outcomes pertinent to stroke rehabilitation. They were chosen as they are valid, reliable, relevant to the population and intervention studied, and simple to use.

1.5.1 Impairment

* Motricity Index (Appendix 1.1)

The Motricity Index is a simple measure of motor loss which was developed for use after stroke[9]. It is a clinical assessment of muscle strength and is based on the Medical Research Council (MRC) grades of muscle power. In the arm, shoulder abduction, elbow flexion and pinch grip are assessed. In the leg, the assessment is of hip flexion, knee extension and ankle dorsiflexion. The Motricity Index is sensitive to changes seen in recovery after stroke, and its validity and reliability have been demonstrated in these patients[70].

* Shoulder Shrug Test (Appendix 1.2)[71]

This is assessed by asking subjects to 'shrug' their shoulder against resistance and is scored on a scale of 0 to 2. A score of 2 indicates full movement and strength against resistance, 1 reduced strength and movement, and 0 no movement at all. Ability to shrug the hemiplegic shoulder has been shown to be a good prognostic indicator for the recovery of hand movements after stroke[72].

Brunnstrom Fugl-Meyer (F-M) assessment (Appendix 1.3)

This is a cumulative numerical scoring system which was designed to assess the development of motor function and balance in stroke patients. Although it is a general motor assessment scale, it has a section specific to the arm[73]. It has been shown to be a valid test in hemiplegic stroke patients with good inter-rater reliability[74] but is time-consuming.

Grip Strength (Appendix 1.4)

This is a sensitive measure of recovery, and is useful prognostically after a stroke[75]. It is measured by asking subjects to squeeze a hand-held dynamometer.

Rivermead Motor Assessment[76] (Appendix 1.5)

This is a widely used measure of motor function after stroke. The scale assesses both impairments and disabilities, but has proven reliability and validity in stroke patients. It is a long test to perform, but can be used more rapidly if the gross function section is assessed simply by asking[77].

*Star Cancellation Test of visuospatial impairment (Appendix 1.6)

This is one of 6 pencil and paper tests from the Behavioural Inattention Test[78]. The stimuli in the test are 52 large stars, 13 letters, and 10 short words, interspersed with 56 smaller

stars. Subjects are asked to mark all the small stars that they can see on the page. Two of the central small stars are used for demonstration, so the maximum score on this test is 54. Its sensitivity as a measure of neglect in stroke patients has been proven[79, 80]. The presence/absence of visuospatial impairment is important in rehabilitation (its presence is associated with poor functional recovery). Visuospatial deficits may also be improved by rehabilitation techniques.

Modified Bobath Assessment Chart[81, 82] (Appendix 1.7)

This involves the use of a standardised chart to evaluate active movements. The tests are designed to give information about a subject's ability or inability to perform certain movements, and they can also be used to monitor progress. There are tests relating to the arm and shoulder girdle, and to the wrist and fingers. There are also sections for the evaluation of lower limb movements. The evaluations are performed with the subject in supine, sitting, and standing positions, and are divided into 3 grades depending on their degree of difficulty (grade 1 being the easiest). It has been shown to be reliable in hemiplegic patients[83], and it has been partially validated (i.e. its validity is based on the fact that stroke subjects move through apparent stages in recovery which make up the "Bobath" approach, rather than on a comparison with a known "gold standard")[84].

1.5.2 Disability

1.5.2.1 Upper limb disability

One approach to testing disability is to measure the subject's performance on one single skill. There are also a number of test batteries that have been developed to test different skills.

Peg Tests (Appendix 1.8)

There are various peg tests which involve timing the patient placing and/or removing a set number of pegs into holes. They are simple to perform and sensitive to changes at the upper level of performance, but not when the disability is severe. They are very good measures of manual dexterity, however they cannot detect loss of proximal strength and may be affected by cognitive and visuospatial problems. The Nine-hole peg test is probably the most simple to perform and is a valid and reliable test in stroke[70, 85]. It has been used in a large randomised controlled trial of upper limb therapy after stroke[53].

Box and Block Test (Appendix 1.9)

This is a timed test of transferring blocks from one part of a box to another. It has been shown to be both a reliable and valid test in elderly people[86]. It has been used in stroke patients[87, 88] and has also been used to study deterioration in those with multiple sclerosis[89].

*Frenchay Arm Test (FAT)[8] (Appendix 1.10)

The FAT is a test of arm function comprising 5 tasks. It is a valid and reliable test in stroke[2], and assesses proximal control and dexterity. It is simple to perform but requires equipment, and although it is sensitive, patients do tend to either pass or fail all of the tests. It has been found to be closely correlated to the F-M score[74].

*Action Research Arm Test (ARAT)[6] (Appendix 1.11)

This is an abbreviated form of test battery first devised in 1965[90] and assesses proximal and distal upper limb functional activity[6]. Its validity and reliability have been proven in stroke patients[7]. It consists of 19 tasks which are grouped into 4 components of arm function: grasp, grip, pinch grip and gross motor movements. Each task is awarded a score from 0 to 3 depending upon the speed and degree of completion. The maximum score is 57. The ARAT has been shown to be well correlated with the F-M score and takes less time to administer[91].

1.5.2.2 Global disability

This is measured in terms of physical interactions (personal, domestic and 'outside home' behaviour) and information transfer (communication, memory, orientation, social interaction)[44].

Activities of Daily Living (ADLs) refer to the basic physical functions which underlie normal living. Measures of ADL should record a person's actual performance rather than their presumed potential ability. 'Extended' ADL scores are intended to cover other categories in addition to 'personal' ADLs such as shopping and housework, although sometimes there is a degree of overlap and it can be difficult to ascertain what activities should come under the term 'ADLs' and what should be classified as 'EADLs'.

*Barthel ADL Index (Appendix 1.12)

The Barthel ADL Index includes the most common areas included within ADL scales, particularly covering continence which other scales omit[92, 93]. The original scoring of the index was 0-100 in 5 point increments[92], but the most commonly used scoring now is 0

(dependent on all items) to 20 (independent)[94] which can always be multiplied up if percentage scores are desired. It consists of the following domains: bathing, stairs, dressing, mobility, transfer, feeding, toilet use, grooming, and continence. It does not however include any direct assessment of cognitive and communicative function. This index has been well validated and the score correlates with motor loss after stroke. A low score predicts a poor outcome after stroke. The score has also been shown to be reliable in a variety of settings, and it is very simple to use[94].

Rivermead ADL Test (Appendix 1.13)

This is a simple ADL test which measures only domestic activities. It has 15 items split between 2 household domains, and is scored on a 7 point scale. It was developed for use with stroke patients in a specialist rehabilitation centre and has been shown to be a reliable and valid test for stroke[95, 96].

Functional Independence Measure (FIM)

In the 1980s, the FIM was developed by a consortium from the American Congress of Rehabilitation and the American Academy of Physical Medicine and Rehabilitation[97]. It measures 18 items over 6 different domains: self care, sphincter control, mobility, locomotion, communication, and social cognition. The individual is given a score of 1 to 7 on each item in each domain. A score of 7 is achieved if the individual is able to perform the task independently. It has been shown to be valid and reliable in a variety of patient groups, including the elderly and those undergoing neurorehabilitation[98, 99].

Functional Assessment Measure (FAM)

The FAM was developed specifically for use in brain injury. It is to be used with the FIM (known as the FIM+FAM (Appendix 1.15))[100], adding a further 12 items to it which address cognitive and psychosocial issues. The FIM+FAM was developed to try to improve reliability for these particular issues which tend to be more subjective and difficult to score[101].

Motor Assessment Scale (MAS) (Appendix 1.17)

The MAS was designed to measure the functional capabilities of stroke patients and focuses mainly on disability. It consists of 8 different items representing 8 areas of motor function and one item relating to muscle tone on the affected side[102]. It is a long test to perform but has been shown to be reliable and valid in stroke patients[103]. The Modified Motor Assessment Scale (MMAS) is a shorter, more simplified version of the MAS. It was modified to increase the assessment's sensitivity to changes in patient status and has been shown to be a reliable test in stroke patients[104].

Health Assessment Questionnaire (HAQ) (Appendix 1.18)

This questionnaire was designed for use in rheumatological diseases[105], although much of it also applies to those with neurological disability. It is to be self-completed which may prove difficult in those with cognitive and communicative problems, more likely in neurological than in rheumatological disease.

Frenchay Activities Index (FAI) (Appendix 1.16)

This was initially designed for use in older people following stroke and has since been revised[106]. It is a 15-item questionnaire which covers domestic, social and leisure activities. It is clinically relevant and simple to use, and can be administered as a postal questionnaire[107]. It has good construct validity, particularly in middle-aged and elderly people, and is reliable for use in stroke patients[108, 109].

*Nottingham EADL Index (Appendix 1.14)

This is an extended ADL index consisting of 22 items split into 4 sections, each of which has been found to form a hierarchal scale in stroke patients[110]. The sections are: mobility (indoor and outdoor), domestic tasks, kitchen tasks and leisure activities. It is simple to administer and can be used as a postal questionnaire. It has also been shown to be reliable and valid in patients with multiple sclerosis[111].

The Rankin Scale

The Rankin Scale is a simple index with 5 categories but is insensitive, is often subjective, and measures impairment and disability as well as handicap[112]. It was developed in 1957 on the basis of research on the prognosis of stroke patients. It measures independence in tasks rather than performance of them. The *Modified Rankin (Appendix 1.19) has 6 categories (the additional category grades those with no disability) and was used in a study of stroke patients in 1988[113]. The authors of this study suggested that a reduction in the number of grades would improve its reliability but that this would be at the expense of its sensitivity.

1.5.3 Quality of life

Quality of life is hard to define which makes it very difficult to measure. In its original meaning, it was related to subjectively perceived emotions of satisfaction and happiness[114]. Quality of life not only reflects subjects' health status but also how they perceive and react to it, and to other non-medical aspects of their lives[115].

In stroke research, 5 of the most commonly used instruments to measure quality of life are:

*Nottingham Health Profile[116] (Appendix 1.20)

This consists of questions divided into 2 parts. The first part contains 38 items which measure subjective health in 6 domains; sleep, pain, emotion, energy, social isolation and mobility. The second part explores the impact of perceived health problems on 7 areas of everyday life; work, home maintenance, home life, sex life, interest and hobbies, social life and holidays. It uses weighted scores to give a scale of 0-100. It has been shown to be valid and reliable in a range of patient groups, and is a useful measure of quality of life after stroke[117]. It has, however, been criticised for not including some areas that may impact on quality of life after stroke e.g. bladder issues, memory problems and financial difficulties.

Short Form-36 (SF36)[118] (Appendix 1.21)

This 36-item survey was developed in 1993 and was designed for self-administration. From the 36 items, eight health profiles are derived from summarised scores. All the dimensions are independent of each other. It is widely used to measure health status after stroke but its validity in this setting has not been proven[119].

Stroke Specific Quality of Life Scale (SS-QOL)[120] (Appendix 1.22)

This was devised to measure health related quality of life in stroke patients. The domains and items, developed from focused interviews with 34 stroke patients, are: energy, family roles, language, mobility, mood, personality, self-care, social roles, thinking, upper extremity function, vision, and work/productivity. Initial results regarding its reliability and validity have been encouraging but further studies in larger stroke populations are needed to assess this further.

Stroke Impact Scale (SIS)[121] (Appendix 1.23)

This is a self-report measure that includes 64 items and assesses 8 domains (strength, hand function, ADL, mobility, communication, emotion, memory and thinking, and participation in activities). It has been shown to be both reliable and valid in stroke patients[121-123].

EuroQoL EQ-5D questionnaire[124] (Appendix 1.24)

This is a generic measure of health status developed by the EuroQoL Group, an international research network established in 1987 by researchers from Finland, the Netherlands, Sweden and the United Kingdom. The questionnaire defines health in terms of 5 domains; mobility, self-care, usual activities, pain or discomfort, and anxiety or depression. Each is subdivided into 3 categories which indicate whether the respondent has no problem,

a moderate problem or a severe problem. A higher score indicates a poorer quality of life. It has been shown to be valid and reliable in a range of patient groups[125, 126].

1.5.4 Upper limb pain

*5-point severity scale and 0-10 numerical rating scale[127, 128] (Appendix 1.25)

Numerous scales are available for measuring pain. A simple descriptive scale can be used, such as the 5-point severity scale, which uses points based on verbal description (i.e. none, mild, moderate, severe, very severe). One of the limitations of this scale is its insensitivity in detecting relatively small changes. The sensitivity can be increased by using numerical rating scales (either 0-10 or 0-20). These 2 types of pain scales have been shown to be well correlated[127].

Visual Analogue Scales[128] (Appendix 1.26)

A Visual Analogue Scale (VAS) is a measurement instrument that tries to measure a characteristic or attitude that is believed to range over a continuum of values and cannot easily be directly measured e.g. the amount of pain that a patient feels. A VAS is usually a horizontal line, 100mm in length, with word descriptors at each end e.g. no pain and very severe pain. The patient marks on the line the point that they feel represents their perception of their current state. The VAS score is determined by measuring in millimetres from the left end of the line to the point where the patient marks. Visual analogue scales are used for the subjective measurement of pain, mood and health status after stroke. A study by Price et al, however, showed that many stroke patients are unable to successfully complete such scales[129].

* Pain-free range of humeral lateral rotation[130, 131]

Some studies have assessed pain at the shoulder by measuring pain-free range of motion[130, 132]. The limitation of this method, however, is its lack of sensitivity to non-mechanical pain (e.g. central post-stroke pain) and concerns about other influences on range of movement (e.g.viscoelastic changes, muscle tone).

1.5.5 Summary of upper limb rehabilitation

- There are many interventions that aim to improve upper limb function following stroke but the literature is unclear about their effectiveness.
- As the majority of functional recovery occurs within the first six months after stroke, the maximum opportunity to improve recovery is offered by early intervention.

- A variety of scales are available for measuring outcomes. In selecting scales, it is important to consider what is to be measured, in what type of problem, and in which particular setting. The chosen scales must also be valid, reliable, relevant to the rehabilitation intervention, and feasible to use.

1.6 Electrical Stimulation (ES)

Electrical stimulation (ES) is defined as using an electric current to excite nerve or muscle tissue. Research studies suggest that treating stroke patients with various forms of electrotherapeutic agents may stimulate lower motor neurons of the peripheral nerve, improve contractibility of type A and c muscle fibres, decrease tone (spasticity) and enhance sensory stimulation[133]. ES may also reduce pain by the gate control theory[134] which is based on the fact that small diameter nerve fibres carry pain stimuli through a 'gate mechanism' but larger diameter nerve fibres going through the same gate can inhibit the transmission of the smaller nerves carrying the pain signal. It is thought that the 'pain gate' can be shut by stimulation of mechanoreceptors and by the release of endogenous opioids, both of which may occur as a result of ES application.

Electrical stimulation may also provide afferent stimulation of the somatosensory cortex by augmented sensory feedback (appropriately timed sensory stimulation to trigger voluntary motor activity), and by proprioceptive afferent stimulation as a consequence of movement and muscle activation mediated by electrical stimulation[135]. Therapeutic electrical stimulation (TES) aims to reduce motor impairment through motor re-learning. Repetitive movements induced by electrical stimulation may be important for motor re-learning in the same way that active repetitive movements are. However, other effects such as muscle strengthening and modulation of spasticity may also influence the motor re-learning process.

A secondary advantage might be the correct alignment of articular surfaces which may be important in the prevention of pain and creating the right conditions for useful limb function.

1.6.1 Types of ES

Electrical Stimulation can be broadly divided into 2 groups: functional electrical stimulation (FES) and therapeutic electrical stimulation (TES). Liberson and colleagues[136] defined FES as 'the use of electrical stimulation to produce muscle contractions that have a functional purpose,' e.g. the stimulation of dorsiflexion to assist gait. TES is designed to have

therapeutic effects which persist after the stimulation is terminated. There is, however, a considerable amount of overlap between FES and TES i.e. although the main objective of FES is for a functional purpose, many applications of FES are associated with long-term therapeutic effects. In addition, TES may produce muscle contractions as with FES, but the main aim of TES is for therapeutic effect rather than functional purposes.

The main application of electrical stimulation for the upper limb following stroke is TES. It has been proposed as a safe method of improving upper limb outcome by enhancing shoulder joint alignment, muscle strengthening, analgesia, and modification of visuospatial deficits[82, 137-141]. TES can be classified into 4 different methods:

1. Neuromuscular electrical stimulation (NMES)
2. EMG-triggered electrical stimulation (EMG-stim)
3. Positional feedback stimulation training (PFST)
4. Transcutaneous electrical nerve stimulation (TENS)

Each of these methods are applied by different devices and can be set to different stimulation parameters to determine the type of reaction provoked by the stimulation. TENS produces continuous or burst stimulation and there is no ramp-up or ramp-down time. The other three methods produce cyclic stimulation and the ramp-up, ramp-down and duty cycle can be adjusted independently.

Patients receive NMES passively whereas they are actively involved in EMG-stim and PFST. NMES is used on innervated muscle to recruit motor units and increase the strength of the muscle, decrease spasticity through reciprocal innervation, improve range of motion, and improve muscle endurance by increasing aerobic capacity of the muscle. EMG-stim facilitates patterned, repetitive, volitionally initiated exercises of the hemiparetic limb and provides cutaneous, proprioceptive, and electrical stimulation feedback with each attempted movement. The electrical stimulation is initiated voluntarily by EMG signals from the target muscle, rather than applied passively by the stimulator[142]. The technique may be used with stroke subjects who can voluntarily generate electromyographic signals in their paretic muscles, but who are unable to generate sufficient muscle contraction for adequate exercise or functional movements. Theoretically, the basis for EMG-stim is that alternative motor pathways can be recruited and activated to assist the stroke-damaged efferent pathways.

In PFST, positional feedback and electrical stimulation are combined to facilitate movement[143]. The onset of electrical stimulation occurs with each voluntary effort and

causes muscle contraction and completion of full joint motion. Through the use of audio and visual displays, the subject is provided with sensitive and immediate sensory feedback of joint motion, a means of comparing their joint position with established goals for motion, and positive reinforcement of goal attainment.

TENS was originally used for the treatment of pain by evoking a sensory reaction without muscle contraction. However, muscle contraction can be produced with TENS in addition to a sensory reaction by adjusting the stimulation parameters[62].

1.6.2 History of ES

The first clinical application of ES was reported by Liberson and colleagues in 1961[136]. They reported a series of case studies using a peroneal stimulator to activate the ankle dorsiflexors during ambulation in 7 hemiplegic patients with gait difficulties due to foot drop and equinovarus. The stimulator was activated when the foot was lifted off the ground. The authors found improvements in ankle dorsiflexion and eversion during the swing phase of gait. The application of ES on the upper limb was first performed by Long and Masciarelli who created an electrophysiologic splint for the hand in 1963 in patients with spinal cord injury[144]. In 1973, the first commercially available FES unit for finger extension in hemiplegic subjects became available[145].

During the 1970s, there were further reports about the use of ES in hemiplegic subjects although the majority of these evaluated the ES technology rather than testing the efficacy of the stimulation[146, 147].

In the late 1970s, the use of FES to produce ambulation in subjects with spinal cord injury was reported[148], and virtually all of the technological improvements in ES in the 1980s were in patients with spinal cord injury.

During the 1990s, there was increased interest in the use of ES in hemiplegic subjects. Much more work was done on the use of ES for the lower limbs (most commonly dorsiflexion assistance during ambulation[149, 150]) than for the upper extremities. The first study utilising an experimental design to evaluate the efficacy of FES in improving gait was undertaken by Bogotaj et al in 1995[151]. Twenty hemiplegic patients within 1 year of stroke were randomly assigned to one of two groups. All received conventional therapy for 6 weeks but one group received FES during the first 3 weeks, and the other during the last 3 weeks of therapy. Outcomes were in terms of gait performance and motor impairment (Fugl-Meyer score[73]).

The authors report greater improvements when patients received FES plus conventional therapy rather than conventional therapy alone, but it is unclear whether these results were statistically significant, so they must be interpreted with caution.

1.6.3 The sNMES regime

Previous trials have used different sNMES regimes (Table 3) and there has been no published review of this to date to provide guidance on which regimes are most effective clinically. It is possible that failure of sNMES to produce clinical benefit in certain trials may be because of the regime used rather than the sNMES itself.

1.6.4 Side effects of sNMES

Surface NMES has been well-tolerated in previous trials. Most trials have reported no dropouts (Tables 1 & 2) and very few side effects from the stimulators. The most common reported side effect is pain at the application site.

1.6.5 Therapeutic applications of ES to the upper limb in stroke subjects

ES has been proposed as a safe method of improving outcome following stroke via mechanisms such as muscle strengthening, improvement in joint alignment (in particular treatment/prevention of shoulder subluxation), analgesia, modification of visuospatial deficits, and psychological benefit due to sensory feedback[5, 62]. The two commonest techniques used in this clinical setting are TENS and NMES. Studies to evaluate the use of ES to the upper limb in stroke patients have looked at its effect to the shoulder, wrist and fingers on a variety of outcome measures such as impairment, function, shoulder subluxation and pain.

The randomised controlled trials (RCTs) of ES in stroke patients are discussed in detail below. The search strategy is detailed in Appendix 3.1.

1.6.6 Randomised controlled trials (RCTs) of electrical stimulation (ES) in stroke subjects

Studies have looked at the effect of electrical stimulation on motor performance, function, shoulder subluxation, pain, spasticity and neglect. There is a mixture of evidence about the effectiveness of any form of electrical stimulation, however it appears that more benefit occurs when muscle contraction is induced[62, 82, 132, 133, 152] (Table 3).

The methodological quality of these studies is variable. Many only recruited small numbers of subjects, and some did not adequately report the population screened, the randomisation method, or the presence/absence of blinding (Tables 1 & 2). The Scottish Intercollegiate Guidelines Network (SIGN) methodology checklist for RCTS (Appendix 3.2) was used to assess methodological quality. Power calculations are not included in this checklist, and are in fact rare in rehabilitation studies. Many such studies are exploratory, and a small sample but with a very significant finding could be important. However, it must be noted that it is often difficult to interpret and generalise the findings of such small studies.

1.6.6.1 ES to the upper limb for motor/functional recovery

Few studies have looked at motor and functional recovery following electrical stimulation to the shoulder after stroke.

In 1994, Faghri et al looked at the effects of functional electrical stimulation (FES) on shoulder subluxation, arm function and recovery, and shoulder pain in hemiplegic stroke subjects[82]. They undertook an RCT of 26 subjects with shoulder muscle flaccidity/paralysis due to stroke but the authors do not state where these were recruited from (i.e. whether they were in-patients or out-patients). They excluded those with a permanent pacemaker, but it was unclear whether there were any other exclusion criteria, for example, subjects with previous shoulder problems. It is also unclear how many were screened for entry into the study.

Thirteen of the participants were randomised to the treatment group and 13 to the control group. The randomisation method is not stated. Those in the treatment group were given 6 weeks of FES to the shoulder (posterior deltoid and supraspinatus) for 1.5-6 hrs per day. It is unclear how much treatment was actually received and there was no sham treatment for the control group.

Participants were assessed at baseline in terms of arm function (using the shoulder and arm function subsection of the modified Bobath assessment chart[81]), arm muscle tone (0-4 grading)[153], posterior deltoid muscle electromyographic (EMG) activity, upper arm girth, shoulder lateral range of motion (SLROM)[130, 131] for assessment of pain in the involved shoulder, and shoulder subluxation (x-rays of both shoulders). These assessments were repeated at 6 and 12 weeks and it is unclear whether or not they were blinded.

At baseline, the subjects were well matched in terms of sex, age, time post-stroke and side of impairment. The mean (+/-SD) time post-stroke was 16+/-5 days in the intervention group and 17+/-4 days in the control group. The majority of subjects had left sided impairments (this may be due to receptive problems in patients with right sided impairments but this is not discussed in the paper, and receptive dysphasia was not given as an exclusion criterion). The authors assumed that the number of current infarcts was similar between groups as the patients were 'randomly assigned'. There were no significant differences between groups in terms of the baseline upper limb assessments, although no results are given for initial upper arm girth.

At 6 weeks, the intervention group had increased arm function, tone, and EMG activity which was statistically significantly higher than the control group. Both groups showed improvements in these measures from baseline to 6 weeks, but these changes were not statistically significant in either group. The 12-week outcomes for function, tone and EMG activity are not reported. At 6 and 12 weeks, there were statistically significant increases in SLROM (both absolute values and when compared with baseline) for patients in the intervention group compared with controls. An increase in the SLROM was interpreted to mean that patients had less pain in the shoulder. There was less subluxation (when compared with baseline) in the intervention group at both 6 and 12 weeks compared with controls. However, this difference was only statistically significant at 6 weeks.

The authors concluded that FES can reduce shoulder subluxation after a stroke and may result in faster recovery of arm function. They suggest that the ES treatment may have resulted in faster recovery of shoulder function by preventing the disuse atrophy that may occur during the flaccid stage of recovery. However, the reduced subluxation in the intervention group was only statistically significantly different from the control group at 6 weeks; this significant difference was no longer present at 12 weeks. Also, the improvement in arm function seen at 6 weeks was not significantly greater than improvements seen in the control group, and the 12-week outcomes for arm function are not reported. The authors also reported that FES can reduce pain at the affected shoulder. However, it is important to note that shoulder pain at baseline is not assessed in this study.

Other studies have looked at recovery following stimulation of the wrist and finger extensors in the paretic arm post-stroke.

In 1979, Bowman et al[143] undertook a randomised controlled study of positional feedback stimulation training (PFST). The aim of the study was to compare a group of hemiplegic

subjects with poor wrist extensor control receiving PFST and conventional therapy with a similar group of subjects receiving only a conventional therapeutic programme. Subjects were recruited between 3 weeks and 4 months post-stroke (embolic or thrombotic) and had a minimum of 5 degrees and maximum of 30 degrees of active extension at the wrist. They had to have sufficient cognition to follow instructions and give informed consent. It is unclear where subjects were recruited from or how many were screened. Randomisation was by the flip of a coin, 15 into the intervention group and 15 controls. Those in the intervention group received PFST for 30 minutes twice daily, 5 times per week for a total period of 4 weeks. There was no sham treatment for those in the control group.

Baseline evaluations were undertaken, and then blinded outcomes performed weekly until the end of the 4 week treatment period. Average maximal isometric wrist extension was measured with the wrist positioned in 30 degrees of flexion and then in 30 degrees of extension (mean of 3 efforts). An electrical goniometer was used to measure voluntary patterned and selective ranges of motion (ROM) at the wrist. In addition to these 2 evaluations, the intervention group were tested weekly with the PFST equipment to determine the patient's ability to extend isotonically against incremental resistances (using 4 resistance levels).

There were no significant differences between the groups at baseline in terms of the above evaluations. No baseline demographics or clinical features were given, however, so it is not possible to comment on whether the subjects in each group were similar. For subjects in the treatment group, there were increases in isometric wrist extension (both in flexion and extension) over the period of the study. Statistically significant differences were seen in the 2^{nd}, 3^{rd} and 4^{th} weeks when the wrist was positioned in 30 degrees of flexion, and the 3^{rd} and 4^{th} weeks when the wrist was in 30 degrees of extension. For ROM, the authors report that the groups were 'essentially equal' at baseline but do not give results for this. The average change in active extension ROM in the treatment group in the 2^{nd}, 3^{rd} and 4^{th} weeks was higher when compared with controls, and this difference was statistically significant in the 2^{nd}, 3^{rd} and 4^{th} weeks. When testing those in the intervention group against resistance, subjects were able to extend against a statistically significantly greater resistance at the end of the treatment program compared with prior to treatment.

The authors state that they felt that establishing performance goals helped patient motivation. They also point out that the PFST equipment in this study was designed to operate automatically, allowing the therapist to oversee the treatment without constantly being present.

In 1998, Chae et al performed a RCT to assess the efficacy of neuromuscular stimulation (NMES) in enhancing motor and functional recovery of the upper limb in acute stroke patients[154]. They state that the design was influenced by the review by Glanz et al (1996)[4] which concluded that further blinded research with longer follow-up periods was needed to look at electrical stimulation in post-stroke rehabilitation.

Subjects admitted to an acute inpatient rehabilitation service within 4 weeks of stroke were screened for inclusion into Chae's study. It is unclear how many subjects were screened, but a total of 46 patients were recruited. Only those with moderate/severe upper limb paresis were included (Fugl-Meyer (F-M) score[73] <44) and there were other exclusion criteria. The participants were randomised to the treatment or control group by a computer-generated random number table.

There were a large number of drop outs (n=17) either because they could not tolerate the stimulation (n=8), did not finish the treatment protocol and declined further treatment (n=5), were medically unstable (n=3), or were found not to have had a stroke (n=1). There was one further drop out in the control group because it was not possible to achieve cutaneous stimulation without muscle activation in this particular subject. Therefore only 28 subjects completed the study-14 in the treatment group and 14 in the control group. Of the 18 subjects who dropped out of the study after randomisation, 11 were in the treatment group and 7 in the control group. Those in the treatment group received NMES for 1 hour per day for a total of 15 sessions. The NMES produced full wrist and finger extension in the treatment group. Those in the control group were given a cutaneous stimulator.

It is of note that only those who completed the treatment were included in the baseline and outcome analyses (i.e. the authors did not use an intention-to-treat analysis). Assessments were undertaken at baseline, and blinded outcomes after treatment, at 4 weeks and at 12 weeks. Motor function was assessed with the F-M score[73] and upper extremity disability assessed with the self-care component of the Functional Independence Measure (FIM)[97] (which is not specific to the upper limb).

At baseline, the 28 subjects who completed the study were well matched in terms of sex, age, past medical history, and side of hemiparesis. The mean (+/-SD) time of stroke onset to treatment was 13.6 (+/- 7.1) days in the treatment group and 17.8 (+/- 5.9) days in the control group. All subjects in the treatment group had non-haemorrhagic strokes, whilst 3 of those in the control group had haemorrhagic strokes (it is unclear whether these were

primary intracerebral haemorrhages or haemorrhagic infarcts). This difference was not statistically significant. There were more cortical strokes and more anterior circulation strokes in the control group compared to the intervention group, but again, this difference was not statistically significant.

At baseline, there were lower motor scores (i.e. upper limb F-M scores) in the control group. This may have confounded the results, but the difference did not reach statistical significance. It is not stated whether these are mean or median scores. Outcomes used were gains in the F-M and FIM scores after the 15-day treatment period and at the follow up periods (4 weeks and 12 weeks). There were greater motor improvements for the treatment group compared to the control group at 15 days, 4 weeks and 12 weeks. These differences are reported to be statistically significant but it must be noted that the 95% confidence intervals are very wide (16.2, 0.0 at 4 weeks; 18.9, -0.2 at 12 weeks). The differences in the FIM gain scores between groups were not statistically significant at any of the follow up periods.

The authors concluded that, whilst an improvement was seen in motor recovery, this did not translate into a functional benefit. They acknowledged the large number of dropouts, mainly due to pain from the stimulator (8 out of the 18, 7 of whom were in the treatment group). They suggested that their results should be interpreted with caution and that future studies should use a functional outcome measure that is specific to the arm and more sensitive to the degree of arm hemiparesis.

In 1998, Sonde et al looked at the effect of low-frequency transcutaneous electrical nerve stimulation (low-TENS) for treatment of the post-stroke paretic arm[155].

They undertook a RCT of 44 patients with a paretic arm (F-M score[73] 0-50) due to a first-ever stroke occurring within the previous 6-12 months. It is unclear where subjects were recruited from, and how many patients were screened in total. No exclusion criteria were given. Subjects were randomised by the random number generator method.

All subjects in the treatment group received stimulation of the wrist extensors, and some also had additional stimulation at the elbow and shoulder (although it is not clear who actually received this additional stimulation). The low-TENS treatment was given for 60 minutes, five times per week, for 3 months. There was no sham treatment for the control group.

Outcome measures (unblinded) were performed at the end of the treatment period and consisted of motor function (F-M score)[73], spasticity (Modified Ashworth Scale[156]), pain (Visual Analogue Scale 0-100[128]), and Activities of Daily Living (ADLs) (Barthel ADL Index[92]).

Twenty six subjects were randomised to the treatment group and 18 to the control group. Mean (SD) time since stroke was 9.1 (2.2) months in the treatment group and 8.3 (2.1) in the control group. Subjects were well-matched at baseline in terms of age and side of paresis. There were more males in the treatment group (19 compared to 8 controls) but this difference was reported as being non-significant. The authors did not report Ashworth scores at baseline, and it was also unclear which of the participants actually had pain at the start of the study. Of note, the mean baseline Barthel scores indicated more severe disability in the control group (69.2 +/- 16.6) compared to the intervention group (29.6 +/- 13) and this difference reached statistical significance (p=0.03).

Improvement in motor function was seen in the treatment group as assessed by the change in F-M score from the start to the end of the study. The improvement was statistically significantly greater than that in the control group. The improvement in motor function in the treatment group was also greater in those less severely affected, and in those with the shortest post-stroke time. There was no effect of the low-TENS on pain, spasticity or ADLs. It must be stressed, however, that this study was uncontrolled, the description of stimulation received is unclear, and outcome assessments were unblinded. The positive results reported in this study must therefore be interpreted with caution.

Sonde et al performed a three-year follow-up study on this cohort[157] to assess whether the low-TENS treatment resulted in long-term improvements in motor function, spasticity or ADLs. Twenty eight (18 treatment and 10 controls) out of the original 44 subjects were available for this re-assessment. It is unclear why the remaining 16 could not be followed-up. The motor performance (F-M score[73]) of the affected arm of subjects in both groups had deteriorated. This decline was greatest in less severely affected subjects in the treatment group, where the F-M score was statistically significantly lower at 3 years compared with the score at the end of the treatment period. There was a slight increase in spasticity (modified Ashworth score[156]) in both groups but this was not statistically significant. The average ADL scores (Barthel ADL Index[92]) decreased in both groups and this was statistically significant in the control group. However, the changes in motor performance, spasticity and ADL scores were not actually compared between the groups. The authors concluded that low-TENS treatment started 6-12 months after stroke does not

affect arm motor function 3 years after completion of treatment. They also concluded that low-TENS treatment may result in maintained ADL-scores at 3 year follow-up. Again, these results must be interpreted with caution in view of the original flaws in study design.

In 1998, Francisco et al[158] performed a single-blind randomised pilot study of EMG-triggered electrical stimulation to assess its effect on the arm function of acute stroke subjects. First ever stroke subjects, within 6 weeks of stroke onset, were screened against strict criteria for entry into the study. It is unclear where they were recruited from, or how many were screened. Inclusion criteria were given as: non haemorrhagic lesion on CT or MRI brain scan, a detectable surface EMG signal from the extensor carpi radialis of the hemiparetic arm, and volitional wrist extension in synergy or isolation with muscle grade of less than 3/5. It is unclear whether subjects with a 'normal' brain scan were excluded from the study on the basis of these criteria. Subjects were excluded if they had previous neurological co-morbidity that impaired strength in the affected upper limb, if they were on medications which impaired neuromuscular performance (e.g. antispasmodics, antiepileptics), if they had an insensate affected forearm, if they had a permanent pacemaker, or if they were pregnant. These strict inclusion and exclusion criteria obviously limited recruitment to this study and this was acknowledged by the authors.

Sixteen eligible subjects were randomised by a computer-generated random number table. Seven of these dropped out due to medical instability. Of the remaining 9 subjects, 4 were in the intervention group and 5 in the control group. No information is given regarding the randomisation groups of the dropouts, and the baseline and outcome data only relates to the 9 who completed the study. Participants in the intervention group received twice daily EMG-triggered electrical stimulation (30 minutes per session) to the forearm extensors (surface electrodes were placed on extensor carpi radialis) 5 times per week for the duration of their inpatient stay. There was no sham treatment for those in the control group, but they were given 2 additional 30-minute individual therapy sessions per day.

Blinded outcomes were performed at discharge from hospital (i.e. at the end of the ES treatment) and consisted of the F-M[73] and FIM[97] scores.

The results showed a significant difference in the distribution of lesion laterality between the 2 groups at baseline (all 5 of the control subjects had left hemisphere lesions compared with only 1 of the 4 in the intervention group). The subjects were otherwise well matched at baseline in terms of age, sex, time from stroke onset to admission, and baseline F-M and FIM scores.

Outcomes at discharge were looked at in terms of 'gain' in scores. Those in the treatment group showed statistically significantly greater gains in the upper limb F-M scores and FIM scores than controls. The authors concluded that EMG-stimulation has the potential for enhancing upper limb motor recovery within 6 weeks of stroke onset, and that this enhanced recovery appeared to translate into functional recovery. However, the numbers in the study were small and the length of treatment (and timing of the outcome assessments) was based on length of stay (which was slightly longer in the treatment group than controls, but this difference did not reach statistical significance). The dropouts were not included in any of the analyses. Also, it is difficult to see how widely applicable these results are, as it appears that EMG-triggered stimulation can only really be used in a very select group of acute stroke subjects.

In 1999, Powell et al undertook an RCT to look at the effects of electrical stimulation (ES) of the wrist extensors on impairment of wrist function and on upper-limb disability in subjects undergoing rehabilitation after acute stroke.[152]

Subjects admitted consecutively, with Medical Research Council (MRC) power of wrist extension grade 4/5 or worse, were screened for entry into the study. A total of 60 were recruited but it is unclear how many were actually screened. Recruited subjects were all 2-4 weeks post-stroke, exclusions were given and all had a CT head scan.

Randomisation was by computer-generated random numbers held in sealed envelopes and 30 were recruited to each group. ES was given for 3 half-hour periods daily for 8 weeks to stimulate wrist and finger extension in the treatment group. No sham treatment was given for the control group. Compliance with treatment was recorded in a patient diary.

Blinded outcomes were undertaken at 4, 8, 20, and 32 weeks. These looked at impairment (using a purpose-built device to measure the isometric strength of wrist extension and the active and passive ranges of motion at the wrist); and disability (Action Research Arm Test (ARAT)[6], grip strength[75] and the 9-hole peg test[70, 85]). Other outcomes were spasticity (modified Ashworth scale[156]), visual inattention (star cancellation test[78]), disability (Barthel ADL score[92]), and global handicap (Rankin score[112]).

Participants were recruited a mean (SD) of 23.9 (7.7) days post-stroke in the treatment group, and 22.9 (5.5) days in the control group. The groups were well-matched at baseline in terms of sex, age, abbreviated mental test score (AMT)[159], side of hemiparesis and stroke subtype. Forty eight subjects of the total of 60 completed the study. Dropouts were

due to death (n=3), further neurological events (n=3), and patients declining follow-up (n=6). Of these 12 dropouts, 5 were in the ES group and 7 were controls. The ES was not associated with any significant local discomfort.

Outcomes were assessed in terms of change from baseline. The authors compared the baseline data with those after treatment (i.e. at 8 weeks) and at the end of the follow-up period (i.e. 32 weeks). They do not report their outcomes at 4 weeks and 20 weeks and it is unclear why this is the case. They showed a statistically significant increase in isometric strength of wrist extensors (at a wrist angle of 0 degrees extension) at both 8 weeks and 32 weeks in the treatment group when compared with controls. ES also reduced upper limb disability, as assessed by the grasp and grip subscores in the ARAT[6] at week 8, but the differences between treatment and control were no longer statistically significant at the end of follow-up (i.e. at 32 weeks). There were however no statistically significant differences seen, between treatment and control groups, in change in resting wrist angle, range of passive extension, hand grip strength, 9-hole peg test, star cancellation and Ashworth, Barthel and Rankin scores, from weeks 0 to 8 or weeks 0 to 32. It is questionable how informative the 9-hole peg test was because many subjects were unable to insert any pegs. Nineteen subjects showed good compliance with the treatment, 3 missed occasional sessions and 5 showed poor compliance although the reasons for this in the latter group were not stated.

The authors concluded that cyclic ES of the wrist extensors enhances motor recovery and reduces upper-limb disability, although the reduction in disability is not maintained after the treatment is stopped. However, it must be noted that the only statistically significant results were seen in strength of wrist extension (at 8 and 32 weeks) and in 2 of the 4 subgroups of the ARAT[6] (at 8 weeks only). They suggested that larger scale studies were needed with use of a sham treatment for the control group.

In 2000, Cauraugh et al[88] undertook a randomised trial of electromyography (EMG) - triggered NMES. The aim of the study was to determine its effect on the wrist and finger extension muscles in individuals who had had a stroke more than 1 year previously. They used a modified crossover design, i.e. control patients received the EMG after the treatment period was complete. It is unclear where subjects were recruited from. Subjects had to be able to voluntarily extend the wrist 20 degrees against gravity from a 90 degrees flexion position. Subjects were excluded if they had more than a 75% motor recovery, if there was a history of 'previous neurological deficit' and/or if they were already enrolled in rehabilitation treatment.

A total of 11 subjects were included in the study - 7 in the treatment group and 4 controls. The authors did not state how they were randomised. Those in the treatment group received two 60-minute sessions of EMG-triggered NMES to the wrist and finger extensors 3 times per week for 2 weeks. There was no sham treatment for the control subjects.

The outcome assessments consisted of the Box and Block Test[87], Motor Assessment Scale[102], F-M score[73], reaction time and sustained muscle contraction. The same instrument was used for both the reaction time and sustained muscle contraction tasks: a 25 lb load cell measured the amount of force generated during the isometric wrist extension movements. For the reaction time, subjects were instructed to respond as quickly as possible to the onset of an auditory stimulus by initiating the wrist and finger muscles for an isometric contraction against the platform of the load cell. For the sustained muscle contraction, subjects were instructed to gradually increase their wrist/finger extension force to a maximal isometric contraction and hold that level for 5 seconds. All of the assessments were undertaken at baseline and then repeated after the 2-week treatment period. It is unclear whether or not these outcomes at 2 weeks were blinded.

The mean age, mean time after stroke, and side of lesion were reported for the 11 subjects but it is not possible to say whether treatment and control groups were similar. No other baseline demographics or clinical features were reported. For the Box and Block test, the treatment group increased the number of blocks moved, whereas the control group maintained the same level of performance for both test sessions. This increase seen in the intervention group reached statistical significance. In the treatment group, there was an improvement in sustained force impulses observed during the isometric contraction task, and this improvement reached statistical significance. No statistically significant results were seen with the MAS, F-M score and reaction times.

The authors concluded that there were improvements in functional motor abilities with EMG-stim treatment. However, it should be noted that a very small number of subjects were recruited and there were flaws in the study design.

In 2003, Popovic et al[160], performed a single-blinded randomised study to evaluate the effects of functional electrical therapy (FET) on the paretic upper limbs of acute stroke subjects. They describe the difference between FET and other forms of electrical stimulation, stating that FET 'combines intensive voluntary activation of proximal muscles and patterned multichannel electrical stimulation of distal muscles providing grasp and release functions in the paretic hand'.

They considered 41 acute hemiplegic subjects for entry into the study but only 28 subjects participated. The authors did not state where the subjects were recruited from. Inclusion criteria included first ischaemic or haemorrhagic stroke (confirmed by MRI or CT scanning) between 2 weeks and 6 months previously, ability to give informed consent, and ability to understand how to apply the electrical stimulation. Exclusion criteria were given.

Subjects were divided into a lower functioning group (LFG) and higher functioning group (HFG) based on their ability to voluntarily extend the wrist and fingers against gravity. A random generator was used to select 28 subjects for the study, 16 from the HFG and 12 from the LFG. Subjects were then randomised into a FET and a control group using a random generator. Therefore, the subjects were assigned to 4 groups: FET HFG, control HFG, FET LFG, and control LFG. All subjects participated in 30 minute treatment sessions for a period of 3 weeks. These sessions were either exercise with stimulation (FET group) or exercise only (control group). The authors report that these sessions were given daily as the subjects were in-patients. They also state that subjects in the FET groups occasionally missed FET sessions but never more than 2 days in a row.

The subjects were assessed at the start of the study, and then blinded outcomes undertaken after the 3-week treatment period, and at 6, 13 and 26 weeks. The outcome measures were the Upper Extremity Functioning Test (UEFT)[161] (Appendix 1.27), Drawing Test (DT) (Appendix 1.28)[162], modified Ashworth scale[156] (Appendix 1.29), and Reduced Upper Extremity Motor Activity Log (RUE/MAL) questionnaire[163] (Appendix 1.30).

At baseline, data for the 28 subjects was given for age, time between stroke onset and study entry, paretic side, and stroke type. The time between stroke onset and study entry was similar between groups. However, it is unclear whether there were any statistically significant differences between groups in terms of the remaining baseline data.

There were no statistically significant differences between intervention and control groups at baseline for both the HFG subjects and LFG subjects in the UEFT, DT, Ashworth scale, and RUE/MAL questionnaire.

Differences in absolute outcome were analysed between intervention and control subjects, in each of the HFG and LFG groups. In the UEFT, significant differences were seen between intervention and control subjects at all of the outcome assessment times. In the DT, statistically significant differences were seen at all outcome times except after treatment (i.e. at 3 weeks) in the LFG. The assessment of spasticity using the modified Ashworth scale

was only performed at the start and end of the study. The muscle tone was decreased in all subjects at the end of the study, but the only statistically significant result was seen in the HFG when comparing intervention with control at 26 weeks. The RUE/MAL questionnaire was also only performed at the start and end of the study. The authors reported statistically significant differences between intervention and control groups at 26 weeks in both the HFG and LFG. They also reported significant differences between groups in the change from baseline to 26 weeks. It is of note that at baseline, those in the HFG had higher scores than those in the LFG and these were even higher in the FET HFG than in the control HFG group. These differences were not commented on by the authors, and it is unclear whether they were statistically significant.

The authors concluded that the FET treatment promoted functional recovery (as measured by the UEFT and DT) and reduced spasticity. The most significant differences were seen in the HFG, indicating greater effects of FET in subjects who were less limited in terms of functioning and movement at the start of the study. The authors stated that the RUE/MAL results indicated that the FET was received well by hemiplegic subjects. However, there were differences at baseline which were not discussed in the paper and it is of note that, with the exception of the modified Ashworth scale, the outcome measures used were not well-recognised scales with proven validity and reliability. Also, this was a small study so results should be interpreted with caution.

Other studies have looked at the effects of electrical stimulation to both the upper and lower limbs following stroke.

In 2001, Johansson et al undertook a multi-centre RCT to study the effects of acupuncture and transcutaneous electrical nerve stimulation on functional outcome and quality of life after stroke[(164)].

One hundred and fifty subjects, within 5 to 10 days of acute stroke, were recruited from medical and neurological centres in Sweden although the number of patients actually screened is not stated. All patients had moderate/severe disability (measured by Barthel ADL Index[(92)], 9-hole peg test[(85)] or 10m walk[(165)]) and exclusions were given.

Subjects were randomised with the use of closed envelopes, and stratified by centre to 1 of 3 groups: acupuncture; sensory stimulation with high-intensity low-frequency transcutaneous electrical nerve stimulation (TENS) that induces muscle contractions; and low-intensity high frequency electrostimulation (control group). Forty eight subjects were randomised to the

acupuncture group, 51 to the TENS group and 51 to the control group. Each treatment session was 30 minutes and took place twice weekly for ten weeks (total of 20 sessions). Treatment was given to both the paretic upper limb and lower limb simultaneously. It is unclear whether any stimulation was given at the shoulder. All subjects received usual therapy irrespective of randomisation group.

Blinded outcomes, performed at 3 months and 12 months, consisted of ADLs (Barthel ADL Index[92]), overall motor function (Rivermead Mobility Index[166]), fine motor function (9-hole peg test[85]), walking ability (10m walk[165]), and quality of life (Nottingham Health Profile Questionnaire[116]). Twelve participants had dropped out of the study at the 3-month follow up, and a further 12 at the 12-month follow-up. Therefore, a total of 126 (84%) subjects remained in the study at the 12-month follow-up, and the reasons for withdrawal were given. Only one subject dropped out of the study due to an adverse reaction from the treatment and he/she was in the TENS group.

The subjects were well-matched at baseline in both groups in terms of age, sex distribution, medical history and CT findings. There were no significant differences between the groups at baseline in any of the above stated outcome measures. Although the authors stated that subjects were recruited within 5-10 days, they did not report the mean or median time post-stroke for the patients recruited.

Outcomes were reported as actual measures at 3 and 12 months and were compared between groups. No statistically significant differences were seen between the groups in overall or fine motor function, walking ability or ADLs at 3 and 12 months. Quality of life was also similar in all groups at follow-up. .

The authors concluded that their data did not support the hypothesis that TENS or acupuncture after stroke is beneficial in patients with moderate or severe hemiparesis. They also stated that although their study was the largest of its kind to date, it was still small. They suggested that the study may not have been adequately controlled as those in the control group received a degree of sensory stimulus. They stated that, on the basis of the results, these treatments could not be recommended as standard in the subacute phase for subjects with moderate or severe stroke.

In 2002, Peurala et al looked at whether cutaneous electrical stimulation has a role in the enhancement of sensorimotor function in chronic stroke[167]. Their study was performed with 59 patients with hemiparesis (the degree of motor impairment was not specified) due to

chronic stroke (mean time to stroke 3.3 years (range 7 months - 14 years)). Subjects were recruited to the study during their 'yearly inpatient intensive rehabilitation period'. It is unclear what this period of rehabilitation entailed as no further details are given in the paper. The numbers in each group were unequal: 32 had active treatment in the paretic hand and 19 in the paretic foot; 8 had sham treatment in the hand but none had sham treatment in the foot. The randomisation method was not described. Subjects received twice daily treatment sessions of 20 minutes for 3 weeks.

Blinded outcomes were undertaken after the 3-week treatment period. The outcome measures included the Modified Motor Assessment Scale (MMAS)[104], 'paretic limb function test', limb sensory function (measured by Somatosensory Evoked Potentials (SEPs) and a Visual Analogue Scale[128]) and 10 metre walking speed[165]. Not all measurements were available on all subjects and the authors did not give reasons as to why this was the case. The 'paretic limb function test' is not a validated test of function. It was described by the authors as a clinical evaluation, assessed by picking up a pencil, all fingers extension, pinch, and wrist extension. Scores were given after treatment depending on whether the patient's performance was better, worse or the same as prior to treatment. It is not clear exactly how this was judged.

At baseline, the age and sex distribution were reported for the total 59 subjects, but not for the individual groups. No other baseline demographics were given. Baseline MMAS, limb sensory function and 10m walk speed results were reported for each group but it was not stated whether there were any statistically significant differences between them. No losses to follow up were reported.

In this study, the number of sessions actually given was stated – a mean of 21.6 +/- 6 sessions. However, they did not report whether there were any differences between the groups in terms of treatment received. It is also of note that it was intended that subjects received a total of 42 sessions, so the mean number actually received was less than half of that intended. They report that the mean (SD) number of individual physiotherapy sessions received by the subjects was 10.4 (3) over the 3 week period and, again, this information was not given for the individual groups.

The authors reported improved 10m walk speed in the hand treatment group, and improved MMAS and sensory function in both treatment groups compared with baseline. The difference was statistically significant for the MMAS in foot-stimulated patients, and for the 10m walk and sensory function in the hand-stimulated patients. The authors concluded that

cutaneous stimulation may improve the motor and sensory function of the paretic limb even years after stroke, but did acknowledge the small numbers (particularly in the control group) and that 'no real randomisation was done throughout the project.'

1.6.6.2 Summary of studies of ES to the upper limb for motor/functional recovery

These ten studies are summarised in Tables 1 and 3. There is marked heterogeneity in terms of study size, the intervention studied and outcome measures chosen, which makes comparisons difficult. There is evidence that ES improves motor recovery but it is unclear whether this translates into improved upper limb function and subsequently a beneficial effect on ADLs[154, 155]. The studies by Fransisco, Powell, Cauraugh and Popovic[88, 152, 158, 160] which suggested that the ES improved function have limitations in their study design (see Tables 1 and 3). For example, Fransisco's study[158] was small in number, did not analyse dropouts and had variable treatment periods and outcome assessment times. The studies by Peurala, Johansson, Faghri and Chae[82, 154, 164, 167] showed no benefit of ES on upper limb function. Faghri's study[82] showed a beneficial effect of ES on upper limb pain and shoulder subluxation.

There is also a suggestion that any beneficial effects of ES are not maintained after treatment is stopped[82, 152].

Table 1: RCTs of ES to the upper limb for motor/functional recovery - checklist (SIGN guidelines)[168]

	Faghri	*Bowman*	*Chae*	*Sonde*	*Francisco*	*Powell*	*Cauraugh*	*Popovic*	*Johansson*	*Peurala*
Appropriate, clearly focused question	Well covered	Well covered	Adequately addressed	Adequately addressed	Adequately addressed	Adequately addressed	Adequately addressed	Adequately addressed	Adequately addressed	Poorly addressed
Randomised	Not reported	Adequately addressed	Well covered	Well covered	Well covered	Adequately addressed	Not reported	Adequately addressed	Well covered	Not addressed
Adequate concealment method	Not addressed	Poorly addressed	Well covered	Well covered	Well covered	Adequately addressed	Not addressed	Adequately addressed	Well covered	Not addressed
'Blinded' subjects & investigators	Not addressed	Poorly addressed	Well covered	Not addressed	Adequately addressed	Adequately addressed	Not addressed	Adequately addressed	Well covered	Not addressed
Groups similar at baseline	Adequately addressed	Poorly addressed	Well covered	Adequately addressed	Poorly addressed	Well covered	Not addressed	Poorly addressed	Adequately addressed	Poorly addressed
Only difference between groups is the intervention	Adequately addressed	Poorly addressed	Adequately addressed	Poorly addressed	Poorly addressed	Adequately addressed	Not addressed	Poorly addressed	Adequately addressed	Poorly addressed
Relevant outcomes measured in valid & reliable way	Adequately addressed	Adequately addressed	Adequately addressed	Adequately addressed	Poorly addressed	Adequately addressed	Poorly addressed	Adequately addressed	Adequately addressed	Adequately addressed
% recruited dropped out before study completion	None	Unclear	44% treatment, 28% controls	None	7 of 16 (not analysed)	5 I, 7 C (3 I, & 2 C not analysed)	None	None	8% at 3 months, 16% at 12 months	None
Intention to treat analysis?	Adequately addressed	Adequately addressed	Poorly addressed	Adequately addressed	Not addressed	Not addressed	Not addressed	Adequately addressed	Adequately addressed	Adequately addressed
Results comparable for all sites	Not addressed	Not addressed	Not applicable	Not addressed	Not applicable	Not applicable	Not addressed	Not reported	Adequately addressed	Not applicable
How well does study minimise bias?	+	-	++	+	-	+	-	+	++	-
Is overall effect due to the intervention?	No	No	Yes	No	No	?Yes	No	?Yes	Yes	No
How many subjects?	26	30	46	44	16	60	11	28	150	59
Main characteristics of participants?	Acute stroke	Stroke. Nil else known.	Acute stroke (mainly first ever stroke)	First stroke within 6-12 months	First stroke (within 6 weeks)	Acute stroke (within 2-4 weeks)	Stroke (within 1 year)	Stroke (within 6 months)	Within 5-10 days of stroke	Chronic stroke (mean 3.3yrs)

	Faghri	*Bowman*	*Chae*	*Sonde*	*Francisco*	*Powell*	*Cauraugh*	*Popovic*	*Johansson*	*Peurala*
What intervention is being investigated?	FES to shoulder	PFST to wrist	NMES to wrist and finger extensors	Low-TENS to wrist +/- elbow/shoulder	EMG-trig ES to forearm extensors	NMES to wrist and finger extension	EMG-trig NMES to wrist & finger extensors	FET to hand	Acupuncture/ high intensity low freq TENS/low intensity high freq ES	E.S. to hand; E.S to foot
What comparisons are made?	Treatment vs. no treatment	Treatment vs. no treatment	Treatment vs. placebo	Treatment vs. no treatment	Treatment vs. no treatment	Treatment vs. no treatment	Treatment vs. no treatment	Treatment vs. no treatment	Above treatments	Treatment to hand vs. treatment to foot vs. sham treatment to hand
Length of follow-up	12 weeks	4 weeks	12 weeks	3 months (& 3 years)	Until discharge	32 weeks	2 weeks	26 weeks	12 months	3 weeks
Outcome measure(s) used	SLROM[130, 131], tone[153], function (Bobath)[81], EMG, subluxation	Wrist extension, ROM wrist	F-M[73], FIM[97]	F-M[73], Modified Ashworth[156], VAS[128], Barthel[92]	F-M[73], FIM[97]	ARAT[6, 7], grip strength[75], 9 hole peg test[70, 85], Modified Ashworth[156], Star cancellation[78], Barthel[92] Rankin[112]	Box and Block Test[87], MAS[102], F-M[73], reaction time, sustained muscle contraction	UEFT[161], DT[162], Modified Ashworth[156], RUE/MAL[163]	Barthel[92], Rivermead Mobility[166] index, 9 hole peg test[70, 85], 10m walk[165], NHP[116]	MMAS[104], Paretic limb function test, limb skin sensation (SEPs and VAS[128]), 10m walk[165]
Effect size	p<0.05	p<0.05	p<0.05	p<0.05	p<0.05	p<0.05	p<0.05	Not stated	p<0.05	p<0.05
Study funding	Rehabilitation Research and Development Service of the US Dept of Veteran Affairs	Veterans Administration, and Rehabilitation Services Administration, DOH, Washington DC	Rehabilitation Medicine Scientist Development Program & Physical Medicine and Rehabilitation Education and Research Foundation	Regional Social Insurance Office, Stockholm County Council, Karolinska Institute, Foundation for Stroke Research	NIDDR grant, Kessler Foundation Grant	Scottish Office Home and Health Department	Interdisciplinary Grant Award, Office of Research, Technology & Graduate Education, Univ. of Florida, Foundation for Physical Therapy	Not stated	Swedish National Board of Health and Welfare, van Malmborgs Foundation for Brain Research, Stockholm County Council	Not stated
Does it help answer the key question?	Yes	No	Yes	Yes	No	Yes	No	Yes	Yes	No

1.6.6.3 ES to the upper limb for shoulder subluxation and shoulder pain

In 1990, Leandri et al undertook an RCT to evaluate the effectiveness of high-intensity TENS vs. low-intensity TENS vs. placebo for the treatment of hemiplegic shoulder pain[132]. They recruited 60 subjects (20 in each group) with ischaemic stroke (mean 12 weeks after stroke). It is unclear where subjects were recruited from and how many were screened. All of the subjects had 'motor impairment' but could stand and walk with assistance, and all had shoulder pain. Those with polyarthritis, bony disorders, and 'overt psychological disturbances' were excluded.

Subjects were randomised to receive either high intensity TENS, low intensity TENS or placebo for a 4-week period. The randomisation method is not described. Electrodes were placed on painful areas and treatment sessions were given 3 times weekly for the 4-week period (i.e. a total of 12 sessions). The actual duration of these sessions was not stated. Blinded outcomes undertaken after treatment and 1 month after that assessed 4 passive range of movements (PROMs) at the shoulder[130, 131].

The baseline characteristics of all subjects were similar with no significant differences between groups in terms of age, gender, time since stroke onset, side of paresis and number with shoulder subluxation. Baseline PROMs at the shoulder were also similar between groups.

The outcome measure was expressed as 'improvement' in PROMs. There was a statistically significant improvement in PROMs for subjects in the high intensity TENS group. Subjective reports of pain were also better in this group. There was some improvement in PROMs in the other 2 groups but these did not reach statistical significance.

In 1999, Linn et al looked at whether electrical stimulation (ES) can prevent shoulder subluxation after stroke[133].

This was an RCT of 40 subjects recruited within 48 hrs of admission to an acute stroke unit. Exclusions were given and subjects were randomised by the use of opaque sealed envelopes (20 to the intervention group and 20 controls).

28 sessions per week (each session lasting 0.5-1hour) of ES (to supraspinatus and posterior deltoid) were given to the treatment group for a total period of 4 weeks. No sham treatment was given to the control group. All subjects completed the study although 2 subjects

couldn't have x-rays at the end of the study period as they were unable to travel to the x-ray department.

Blinded outcomes undertaken at 4 weeks and 3 months, were shoulder subluxation (x-ray appearances), pain (pain-free range of passive lateral rotation using a clinical goniometer[130, 131]), motor function (upper arm section of the Motor Assessment Scale[102]) and upper arm girth.

There were no significant differences between the groups at baseline in terms of age, gender distribution, affected side, stroke classification, shoulder subluxation, pain, motor function and upper arm girth. The time from stroke onset is not reported, although it is stated that subjects were recruited within 48 hours of admission.

There was greater subluxation in the control group at 4 weeks compared to the treatment group, although this difference did not reach statistical significance. This difference was not maintained after the withdrawal of treatment (i.e. at the 3-month assessment). There were no statistically significant differences in change in motor score, lateral rotation, pain and arm girth between groups over the total study period (i.e. up to 3 months).

The authors concluded that subluxation was prevented during the ES treatment but then relapsed after the treatment was stopped.

In 1999, Kobayashi et al also looked at therapeutic electrical stimulation (TES) for the reduction of shoulder subluxation[169]. They also aimed to identify which of the 2 major muscles, supraspinatus or middle deltoid, was more effective in improving subluxation and shoulder function.

Twenty four subjects with clinically suspected shoulder subluxation due to chronic stroke were identified from a rehabilitation unit. Seventeen of these, who showed downward shoulder subluxation on a stress x-ray test, were recruited. Exclusion criteria were given. There was no true randomisation method. Subjects were randomly assigned to an S group (who received TES to the supraspinatus muscle) and a D group (who received TES to the middle-deltoid muscle). Subjects who refused electrical stimulation or who were not able to undergo the continuous TES treatment were assigned to the control group.

The treatment groups received TES for 15 minutes twice daily for a period of 6 weeks. There was no sham treatment for the control group. The effect of TES of each muscle on shoulder subluxation during treatment was confirmed using x-ray.

Outcome assessments were undertaken at 6 weeks and it is unclear whether or not these were blinded. These were to assess shoulder subluxation, maximal voluntary abduction force of the shoulder joint and EMGs of each muscle, shoulder pain, and muscle tone of the pectoralis major. To assess subluxation, x-rays were taken while patients were in a seated position, during a no-stress and a stress test. During the no-stress test, subjects kept their arm in a relaxed position, and during the stress test, a 3.5kg weight band was placed around the distal part of the upper arm. The maximum abduction force of the shoulder and EMG recordings were taken while the subject performed three 4-second trials of maximum abduction in a seated position. During this test, subjects were restrained by straps around the trunk to limit elevation, rotation of the scapula, and lateral flexion of the trunk. Shoulder pain was evaluated using a visual analogue scale[128] during the movement of voluntary abduction. Pectoralis major muscle tone was assessed using the modified Ashworth Scale[156].

Six subjects were assigned to the S group, 6 to the D group, and 5 to the control group. The time of stroke to randomisation was very different in each group (mean 60.3 weeks in S, 95.0 weeks in D and 190.2 weeks in the control group). Baseline demographics were similar between the groups. Patients in the D group were older than those in the S and control groups (mean age 69.3 years compared with 59.3 and 53.2 respectively) although it is not reported whether this difference reached statistical significance. No statistically significant differences were seen in the degree of subluxation and maximum abduction force between the 3 groups before the TES was given.

In the stress test, there was decreased subluxation in the treatment groups compared to controls (which was statistically significant in the D group) after 6 weeks. No statistically significant results were seen in the no-stress test. There was an increased mean abduction force in the treatment groups compared to controls, which again reached statistical significance in the D group. Increased EMG activity was seen in both treatment groups but the EMG results for the control group are not reported. Seven subjects had pain at baseline, 3 in the S group, 3 in the D group and one in the control group. Four of the 6 in the TES groups experienced as much as a 50% reduction in pain relief following the TES treatment. Muscle tone was assessed in terms of change from baseline, and muscle tone did not decrease in any of the subjects when assessed at 6 weeks.

The authors concluded that TES treatment reduces shoulder subluxation and also results in an increase in force of contraction and EMG activity of affected shoulder muscles, and a decrease in pain. A comparison of the TES effects of the 2 muscles showed a tendency for deltoid muscle stimulation to be more effective in increasing muscle force. They state that these results thus indicate an improvement in shoulder function by the TES treatment, despite the fact that function is not actually assessed. The limitations of the study were that there were large differences in time from stroke onset between the groups. The randomisation method was questionable. The authors suggest that the efficacy of TES in preventing subluxation should be evaluated for long term use of TES treatment from the early recovery stage.

A study by Chantraine et al in 1999[170] was performed to determine the effect of electrical stimulation on subluxation and shoulder pain in hemiplegic subjects. One hundred and twenty patients were included from a total of 256 hemiplegic subjects followed as inpatients or outpatients at the University Hospital of Geneva. Exclusions were given. Not all were stroke subjects: there were 92 with cerebral thrombosis, 9 with cerebral haemorrhage, and 19 with brain injury. All were within 2-4 weeks of diagnosis, and all had a subluxed and painful hemiplegic shoulder.

Subjects were alternately assigned to either the treatment or control group (i.e. there was no randomisation). Those in the treatment group received ES for 5 weeks; 130 minutes in the first week, then increasing throughout subsequent weeks. This ES was given to the shoulder but the authors do not report to which muscles it was applied. There was no sham treatment for the control group. Subjects were assessed at baseline and then outcomes were undertaken at 1, 3, 6, 12, and 24 months. It is unclear whether or not these assessments were blinded. Shoulder pain was assessed using a Visual Analogue Scale[128] and by recording the presence or absence of pain during active and passive movement of the shoulder[130, 131]. Shoulder subluxation was assessed radiologically. Function was assessed by asking subjects to perform an antepulsion and abduction of their hemiplegic arm. Recovery of motor function was defined as the ability to raise the arm actively to 60 degrees of antepulsion and to 40 degrees of abduction.

The authors state that the groups were similar at baseline but only data regarding age and side of hemiplegia is given. It is of note that subjects in this study were very young (mean 52.7 years in the treatment group and 52.3 years in the control group). The authors report improvement in pain, subluxation, and motor function in the ES group which was maximal at 6 months, and conclude that their work confirms that of other studies showing the beneficial

effect of ES on pain and subluxation in hemiplegic subjects. However, they do not use a validated tool to assess function, and it is difficult to generalise these findings in view of the limitations already described.

In 2000, Wang et al[171] undertook an RCT to assess the effectiveness of a functional electrical stimulation (FES) programme on acute and chronic shoulder subluxation. Thirty two stroke subjects (16 men and 16 women) were recruited from rehabilitation inpatient and outpatient departments. It is unclear how many were screened. All participants had to demonstrate a minimum of 9.5mm of acromiohumeral distance in their affected shoulder. Those with a history of shoulder pain, traumatic lesions to the shoulder joint, limited functional range of shoulder motion, or reflex sympathetic dystrophy syndrome were excluded.

Participants were placed into 2 groups: the short duration (hemiplegia onset within 21 days) and the long duration (hemiplegia onset more than 365 days previously) groups. Sixteen subjects were in each of these groups. The participants were then randomised to either a treatment or a control subgroup (n=8 in each) but it is unclear how this randomisation was done. Those in the treatment group received 6 weeks of FES to posterior deltoid and supraspinatus, followed by 6 weeks of routine therapy, followed by a further 6 weeks of FES. The FES was given 5 times weekly but the duration of these sessions is not stated. There was no sham treatment for the control group.

The outcome was the degree of shoulder subluxation on X-ray. This was assessed at 6 weeks, 12 weeks, and 18 weeks i.e. after both courses of the FES, and after the 6 weeks of routine therapy. It is unclear whether or not these outcomes were blinded.

In the short duration group, the treatment and control subgroups were similar at baseline. There were statistically significant decreases in subluxation (compared with baseline) in the treatment group after both courses of FES, but this was not maintained during the period of routine therapy. In the long duration group, the treatment and control subgroups were similar at baseline. Of note, the degree of subluxation in all of these subjects was statistically significantly greater at baseline compared with those in the short duration group. No statistically significant differences in degree of subluxation were seen in either subgroup of the long duration group at any of the outcome times.

In conclusion, this study demonstrated the benefit of ES in reducing subluxation in acute hemiplegic subjects, but this benefit was not maintained once the stimulation course ended.

It must be noted that this study was very small, and did not report the randomisation method. There was no sham treatment for controls, and it was unclear whether or not outcome assessments were blinded.

1.6.6.4 Summary of studies of ES to the upper limb for shoulder subluxation and shoulder pain

These five studies are summarised in Tables 2 and 3. Again, there is marked heterogeneity in terms of study size, the intervention studied and outcome measures chosen, which makes comparisons difficult. There is evidence of the benefit of ES in reducing shoulder subluxation and shoulder pain from these studies[132, 133, 169-171]. However, it is unclear whether this benefit translates into an improvement in motor function and ADLs, and there is also a suggestion that benefits seen are not maintained after the treatment is discontinued.

1.6.6.5 Other RCTs of ES to the upper limb

In 1998, Tekeoglu et al[172] performed a randomised controlled trial of 60 stroke subjects to look at the effect of transcutaneous electrical nerve stimulation (TENS) on Activities of Daily Living (ADLs). Subjects were between 30 and 240 days post stroke and all were in-patients of a university clinical research programme for hemiplegia after stroke.

All stroke subjects had a hemiparesis, and the diagnosis had been determined by 'physical and laboratory examination including CT and blood screen.' Subjects had to be able to stand and walk with assisted if necessary, and give informed consent for participation in the study. No exclusions were given (e.g. previous neurological deficit).

Participants were randomised to one of 2 groups (30 patients in each group) by block randomisation. Subjects in the treatment group received 8 weeks TENS treatment to the elbow and calf for half an hour per day, 5 days per week (Monday to Friday) i.e. a total of 40 sessions. The sensory threshold was determined by the intensity of stimulation which was gradually increased to the 'bearable level'. Subjects in the control group received a sham stimulator. All subjects in the study received the same type of exercise programme each morning in addition to either active TENS or placebo TENS.

Blinded outcomes were undertaken at 8 weeks (i.e. after treatment). The Barthel Index[92] was used to assess ADLs. Spasticity was also measured using the Modified Ashworth Scale[156].

Baseline characteristics were similar between the 2 groups in terms of age, gender distribution, days post-stroke, side of hemiparesis, and presence or absence of shoulder pain. However the baseline Barthel scores indicate that patients in the treatment group were initially much more dependent than controls, and this was statistically significant.

At 8 weeks, an improvement in ADLs was seen in both groups, but it was more marked (and reached statistical significance in the treatment group. There was a statistically significant reduction in spasticity in both groups at 8 weeks in both upper and lower limbs.

The TENS treatment therefore had a positive effect on ADLs but none on spasticity. However, those in the treatment group were more dependent at baseline which may have confounded the results. As the subjects were recruited from a research programme, it is difficult to generalise these results.

Also in 1998, Hesse et al[173] performed a double-blind randomised controlled trial of botulinum toxin and electrical stimulation in the treatment of upper limb flexor spasticity after stroke. Twenty four subjects between 6 and 11 months after stroke (mean 7.45 months) were recruited to the study. All were outpatients from a neurological rehabilitation clinic. All had severe upper limb flexor spasticity (at least grade 3 on the Modified Ashworth Scale[156]) and a non-functional affected upper limb with no possibility of any selective movement. Exclusion criteria were given. Subjects were randomised to one of 4 treatment groups although the method used was unclear. The 4 groups were: botulinum toxin (botox) and electrical stimulation (n=6), botulinum toxin only (n=6), placebo and electrical stimulation (n=6), and placebo (n=6) only. The botox was to biceps, brachialis and the finger flexors. The electrical stimulation was to the arm and forearm for 30 minutes three times daily during the 3 days following the botox injection. There was no sham treatment for the placebo group.

Blinded outcomes were undertaken at 2, 6 and 12 weeks after treatment to assess muscle tone (Modified Ashworth Scale[156]), limb position at rest, and difficulties encountered by the subject and/or observed by the caregiver with three ADLs.

No baseline demographics or clinical features were reported. The authors conclude that electrical stimulation enhances the effectiveness of botox in treating spasticity. However, there were no differences across the groups for the Ashworth scores of the elbow, wrist and finger joints. The only statistically significant result seen was with regard to the facilitation of hand hygiene (daily activity cleaning the palm) when the combined treatment of ES and botox was superior to placebo and ES, and placebo alone. However, it was not statistically significantly better than treatment with ES and placebo.

Table 2: RCTs of ES to the upper limb for shoulder subluxation/pain, and other RCTs - checklist (SIGN guidelines)[168]

	Leandri	***Linn***	***Kobayashi***	***Chantraine***	***Wang***	***Tekeoglu***	***Hesse***
Appropriate & clearly focused question	Adequately addressed	Adequately addressed	Adequately addressed	Adequately addressed	Adequately addressed	Adequately addressed	Adequately addressed
Randomised	Not addressed	Adequately addressed	Not addressed	Not addressed	Not addressed	Adequately addressed	Not addressed
Adequate concealment method	Not addressed	Adequately addressed	Not addressed	Not addressed	Not addressed	Adequately addressed	Not addressed
'Blinded' subjects & investigators	Adequately addressed	Adequately addressed	Not addressed	Not addressed	Not addressed	Adequately addressed	Adequately addressed
Groups are similar at baseline	Well covered	Well covered	Poorly addressed	Poorly addressed	Adequately addressed	Adequately addressed	Not addressed
Only difference between groups is the intervention	Adequately addressed	Adequately addressed	Poorly addressed	Poorly addressed	Adequately addressed	Adequately addressed	Not addressed
Relevant outcomes measured in a valid & reliable way	Adequately addressed	Adequately addressed	Adequately addressed	Poorly addressed	Poorly addressed	Adequately addressed	Poorly addressed
% recruited dropped out before study completion	None	None	None	4%	None	None	None
Intention to treat analysis?	Adequately addressed	Adequately addressed	Adequately addressed	Adequately addressed	Adequately addressed	Adequately addressed	Adequately addressed
Results comparable for all sites	Not addressed	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not addressed
How well does study minimise bias?	+	+	-	-	-	++	-
Is overall effect due to the intervention?	Yes	Yes	No	No	No	Yes	No

	Leandri	***Linn***	***Kobayashi***	***Chantraine***	***Wang***	***Tekeoglu***	***Hesse***
How many subjects?	60 (20 high intensity TENS, 20 low intensity, 20 placebo)	40 (20 intervention, 20 control)	17 (6 supraspinatus ('S') group, 6 deltoid ('D') group, 5 controls)	120 (60 intervention, 60 control)	32	60 (30 intervention, 30 control)	24 (6 in each group)
Main characteristics of participants?	Ischaemic stroke with shoulder pain	Acute stroke	Chronic stroke	Acute. 101 stroke, 19 brain injury	Acute and chronic stroke	Stroke (in a research programme)	Chronic stroke
What intervention is being investigated?	TENS to shoulder	ES to shoulder	ES to shoulder	ES to shoulder	FES to shoulder	TENS to elbow/calf	Botox & ES to forearm & finger flexors
What comparisons are made?	As above	Treatment vs. no treatment	Treatment vs. no treatment	Treatment vs. no treatment	Treatment vs. no treatment	Treatment vs. placebo	Treatments vs. placebo
Length of follow-up	8 weeks	3 months	6 weeks	24 months	18 weeks	8 weeks	12 weeks
Outcome measure(s)used	Passive range of movement at the shoulder[130, 131]	Subluxation (x-ray), pain free range of movement[130, 131], Motor Assessment Scale (MAS)[102], upper arm girth	Subluxation (x-ray), abduction force, EMG, pain (Visual Analogue Scale[128]), Modified Ashworth[156])	Pain (VAS[128] and range of pain-free motion[130, 131]), subluxation (x-ray), function (antepulsion & abduction of upper limb)	Subluxation (x-ray)	Barthel[92], Modified Ashworth[156]	Modified Ashworth[156], limb position at rest, difficulties with ADLs
Effect size identified	p<0.01	Not stated	Not stated	Not stated	p<0.05	p<0.01	p<0.01
Study funding	Not stated	Scottish Home Office & Health Dept	Not stated	Not stated	National Science Council of the Republic of China Grant; an award from the Medical Research and Advancement Foundation	Not stated	Speywood Pharmaceuticals
Does it help answer the key question?	Yes	Yes	No	No	No	Yes (but not generalisable)	No

Table 3: RCTs of ES to the upper limb in stroke subjects

(* Trials of ES to the shoulder)

Author and year	*No. of subjects*	*Time after stroke*	*Exclusions*	*Randomi-sation method*	*Intervention(I) / Control (C)*	*Follow-up*	*Main outcome measures*	*Summary of findings*
* Faghri, 1994 [82] 'The effects of functional electrical stimulation on shoulder subluxation, arm function recovery, and shoulder pain in hemiplegic stroke patients'	26	Mean 16.5 days Unclear where recruited from	Permanent pacemaker Unclear how many screened	Not known	I - 6 weeks FES (to supraspinatus and posterior deltoid) for 1.5-6hours per day C - no sham	6 and 12 weeks. Unclear whether blinded.	- Pain-free range humeral lateral rotation[130, 131] - Arm function (Bobath assessment[81]) - Tone (0-4 grading)[153] - Radiological glenohumeral separation (mm) - EMG activity	Improved arm function at 6 weeks but not significantly better than controls. Reduced shoulder subluxation and pain at 6 and 12 weeks in the treatment group (but not significant for subluxation at 12 weeks). Shoulder pain not assessed at baseline.
Bowman, 1979 [143] 'Positional feedback and electrical stimulation : an automated treatment for the hemiplegic wrist'	30	3wks-4mths	All had min 5 & max 30 degrees active extension at wrist. Cognition to consent and follow instructions.	Flip of a coin	I – PFST for 30 minutes 2x/daily, 5 times per week for 4 weeks. C – no sham	1, 2, 3, and 4 weeks. Blinded.	- Average maximal isometric wrist extension - Ranges of motion (ROM) at the wrist (electrical goniometer) - No baseline demographics/clinical features given	Significant increase in wrist extension and ROM in the treatment group at 2, 3 and 4 weeks when compared with controls. No longer term follow up done.
Chae, 1998 [154] 'Neuromuscular stimulation for upper extremity motor and functional recovery in acute hemiplegia'	46 (only 28 completed the study)	Within 4 weeks (with moderate /severe upper limb paresis) Unclear how many screened	History of potentially fatal cardiac arrhythmias; demand pacemaker; seizures within 2yrs;active reflex sympathetic dystrophy; residual upper limb weakness	Computer-generated random number table	I - NMES (to produce full wrist and finger extension) 1 hour daily for total of 15 sessions C - cutaneous stimulator	After treatment, 4 and 12 weeks. Blinded.	- Motor function (F-M score[73]) - Upper extremity disability (self-care component of the FIM[97])	Improvement seen in motor recovery which did not translate into functional improvements. Reported statistically significant improvements in motor recovery with treatment but wide confidence intervals. Did not use intention to treat analysis. Large number of dropouts mainly due to pain from the NMES

Author and year	*No. of subjects*	*Time after stroke*	*Exclusions*	*Randomi-sation method*	*Intervention(I) / Control (C)*	*Follow-up*	*Main outcome measures*	*Summary of findings*
* Sonde, 1998 [155] 'Stimulation with low frequency (1.7Hz) transcutaneous electric nerve stimulation (low-tens) increases motor function of the post-stroke paretic arm'	44	6-12 months Unclear where recruited from and how many screened	Not stated	Random number generation	I - 3 months of low-TENS for 60 minutes 5x per week To wrist / elbow / shoulder. All received wrist stimulation. Unclear who received additional stimulation to elbow and shoulder. C – no sham	3 months Unblinded	- Motor function (F-M score[73]) - Spasticity (Modified Ashworth Scale[156]) - Pain (Visual Analogue Scale 0-100[128]) - ADLs (Barthel Index[92])	Improvement in motor function in the treatment group, particularly in those less severely affected and with shortest post-stroke time. No effect on pain, spasticity and ADLs Unclear who had pain at baseline. Note 3 year follow up study showed no long term advantage[157]
Francisco, 1998 [158] 'Electromyogram-triggered neuromuscular stimulation for improving the arm function of acute stroke survivors: a randomized pilot study'	16 Unclear where recruited from and how many screened	Within 6 weeks	Neurological co-morbidity that impaired strength in affected upper limb; on medication which impaired neuromusc. performance	Computer generated random number table	I - 2x30 sessions 5x/week for duration of inpatient stay (to extensor carpi radialis). C - no sham. Received 2 additional 30min therapy sessions per day	At discharge from hospital i.e. end of treatment period Blinded	F-M score[73] FIM[97]	Significant difference in distribution of lesion laterality at baseline Significant increase in F-M/FIM for treatment compared with controls But no longer term outcomes done, small numbers, dropouts not analysed, variable treatment periods and outcome times.
Powell, 1999 [152] 'Electrical stimulation of wrist extensors in poststroke hemiplegia'	60 Power of wrist extension 4/5 or worse. Unclear how many screened	2-4 weeks	Previous wrist problem; unable to understand the study.	Computer-generated random numbers held in sealed envelopes	I - 8 wks ES (to stimulate wrist and finger extension) for 3 x 0.5 hrs per day C - no sham Patient diary to look at compliance	4, 8, 20, and 32 weeks Blinded	Upper limb impairment (purpose-built device to measure isometric strength of wrist extension and active/passive wrist movements) Upper limb disability (ARAT[6, 7], grip strength[75], 9-hole peg test[70, 85])	Report that ES of the wrist extensors enhances motor recovery and reduces upper limb disability although the latter is not maintained after treatment is stopped. But the only statistically significant results are seen in strength of wrist extension (at 8 + 32 weeks) and in 2 of the 4 subgroups of the ARAT at 8 weeks.

Author and year	*No. of subjects*	*Time after stroke*	*Exclusions*	*Randomi-sation method*	*Intervention(I) / Control (C)*	*Follow-up*	*Main outcome measures*	*Summary of findings*
Cauraugh, 2000 [88] 'Chronic motor dysfunction after stroke: recovering wrist and finger extension by Electromyography-Triggered Neuromuscular Stimulation'	11 Randomised trial Modified crossover design	> 1 year	No other neurological deficits; not currently enrolled in rehabilitation treatment	Not known	I - 2 x 60 minute sessions 3 times per week for 2 weeks To wrist and finger extensors C - no sham	2 weeks Not blinded	- Box and Block Test[87] - MAS[102] - F-M score[73] - Reaction time - Sustained muscle contraction	Few baseline characteristics given. Significant improvements in box & block test, and sustained muscle contraction in the treatment group. No significant results for the MAS, F-M, and reaction times.
Popovic, 2003[160] 'Clinical Evaluation of Functional Electrical Therapy in acute hemiplegic subjects'	28 Single-blinded randomised trial Unclear where recruited from	Between 2 weeks and 6 months	Dependent on care for ADLs; severe medical condition/ previous injury or disease in any arm and/or hand; pacemaker	Random generator method	Subjects characterized to higher functioning or lower functioning group (HFG or LFG). I - 30 minutes daily of FET to paretic hand for 3 week period C - no sham	3, 6, 13, 26 weeks. Blinded	- Upper Extremity Functioning Test (UEFT)[161] - Drawing Test (DT)[162] - Modified Ashworth Scale[156] - Reduced Upper Extremity Motor Activity Log questionnaire (RUE/MAL)[163]	In the DT, statistically significant differences seen at all outcome times (except after treatment) in the LFG. Decreased muscle tone in all subjects at the end of the study, but the only statistically significant result was seen in the HFG when comparing intervention with control. In the RUE/MAL, significant differences seen in both the HFG and LFG at 26 weeks.
* Johansson, 2001 [164] 'Acupuncture and transcutaneous nerve stimulation in stroke rehabilitation'	150 Patients with acute stroke. Unclear how many screened	5-10 days	Neurological/ psychiatric disorder; unable to comprehend trial information; in another similar trial; failure to obtain consent	Closed envelopes	I - Acupuncture vs. high-intensity low frequency TENS C - low-intensity high frequency TENS 10 weeks of 30min sessions twice weekly To upper limb and lower limb simultaneously	3 and 12 months Blinded	- ADLs (Barthel Index[92]) - Overall motor function (Rivermead Mobility Index[166]) - Fine motor function (9-hole peg test[85]) - Walking ability (10m walk[165]) - QOL (NHP questionnaire[116])	No statistically significant differences seen between groups in any of the outcome measures

Author and year	*No. of subjects*	*Time after stroke*	*Exclusions*	*Randomi-sation method*	*Intervention(I) / Control (C)*	*Follow-up*	*Main outcome measures*	*Summary of findings*
Peurala, 2002[167] 'Cutaneous electrical stimulation may enhance sensorimotor recovery in chronic stroke'	59 With chronic stroke	7 months to 14 years (mean 3.3 years)	Not stated	Not known	I - Active treatment to hand vs. active treatment to foot. C - sham treatment to hand 20 minutes of cutaneous ES 2x/daily for 3 wks. Looked at amount actually received.	3 weeks Unclear whether blinded	- Motor recovery (MMAS[104], paretic limb function test, 10m walking speed[165]) - Limb sensory function (Somatosensory Evoked Potentials (SEPs) and Visual Analogue Scale (VAS)[128])	Not all measurements available on all participants – reasons for this not stated. Few baseline characteristics given. Significantly improved 10m walk and limb sensation in the hand treatment group. Improved MMAS in foot-stimulated subjects.
* Leandri, 1990 [132] 'Comparison of TENS treatments in hemiplegic shoulder pain'	60 With hemiplegic shoulder pain Unclear where recruited from and how many screened	Mean 12 weeks	Polyarthritis Other bony disorders Overt psychol. disturbances (Patients had to be able to stand and walk if assisted)	Not known	I - High intensity TENS vs. low intensity TENS C – sham stimulation To painful areas 3 x weekly sessions for 4 weeks. Duration of sessions not known	4 weeks 8 weeks (not used) Blinded	- Pain-free range of glenohumeral motion, including lateral rotation[130, 131]	Significant improvement in high intensity TENS group Subjective reports of pain also better in this group
* Linn, 1999 [133] 'Prevention of shoulder subluxation after stroke with electrical stimulation'	40 Recruited within 48hrs of admission to an acute stroke unit	Within 48 hours	No previous pathology to shoulder; adequate communicating ability; permanent pacemaker/ metal in situ; women of childbearing age (because of x-rays)	Opaque sealed envelopes	I - ES (to supraspinatus and posterior deltoid) – 28 sessions (0.5-1hr) per week for 4 weeks C - no sham	4 weeks 3 months Blinded	- Shoulder subluxation (x-ray appearances) - Pain (pain-free lateral rotation and pain scale[130, 131]) - Motor function (upper arm section of Motor Assessment Scale[102]) - Upper arm girth	Significantly greater subluxation in controls during treatment period, but difference not maintained after withdrawal of treatment No significant differences in other outcomes

Author and year	*No. of subjects*	*Time after stroke*	*Exclusions*	*Randomi-sation method*	*Intervention(I) / Control (C)*	*Follow-up*	*Main outcome measures*	*Summary of findings*
* Kobayashi, 1999 [169] 'Reduction in subluxation and improved muscle function of the hemiplegic shoulder joint after therapeutic electrical stimulation'	17 From a rehab unit All with clinically suspected shoulder subluxation due to stroke	Means (weeks): 60.3 in S group 95.0 in D group 190.2 in C group	Previous elective treatment on shoulder; previous history of disease of shoulder; unable to follow instructions; no voluntary movement of shoulder.	No true randomisation method.	I - TES to supraspinatus (S group) vs. TES to middle-deltoid (D group) - 15 minutes 2x/daily for 6 weeks C - no sham (C group)	6 weeks Unclear whether blinded	- Shoulder subluxation (x-ray) - Max. voluntary abduction force of shoulder joint - EMGs - Shoulder pain (VAS)[128] - Muscle tone of pectoralis major (Modified Ashworth Scale)[156]	Reduction in shoulder subluxation (stress test statistically significant in D group at 6 weeks). Significantly increased force of contraction in D group. Increased EMG activity of affected muscles in treatment group but results not given for controls. Decreased pain in treatment groups (unclear whether significant)
* Chantraine, 1999[170] 'Shoulder pain and dysfunction in hemiplegia: effects of functional electrical stimulation.'	120, 101 with stroke, 19 with brain injury. From 256 inpatients or outpatients from the university hospital	2-4 weeks	Subjects with bilateral hemiplegia, or cerebral tumour; previous shoulder pain/trauma, reflex sympathetic dystrophy syndrome.	No true randomisation method. Subjects were alternately assigned to groups.	I - ES to the shoulder C - no sham	1, 3, 6, 12 and 24 months Unclear whether all assessments were blinded.	- Shoulder pain (VAS)[128] and pain-free range of motion[130, 131]). - Shoulder subluxation (x-ray) - Arm function (antepulsion and abduction of hemiplegic arm)	Improvements in all outcome measures compared with baseline, maximal at 6 months. Statistically significantly greater improvements in treatment group compared with controls. Note that measurement of function in this study is not performed using a recognised validated scale.
* Wang 2000[171] Functional Electrical Stimulation on chronic and acute hemiplegic shoulder subluxation.	32 acute and chronic stroke from inpatient and outpatient rehabilitation units	Less than 21 days; more than 365 days	History of shoulder pain, traumatic lesions to shoulder, limited shoulder range of motion, or reflex sympathetic dystrophy syndrome	Not stated	I – FES to shoulder for 6 weeks, followed by 6 weeks routine therapy, followed by further 6 weeks of FES. FES given 5 x weekly. Duration of sessions not stated. C – no sham.	6, 12, 18 weeks Unclear whether blinded.	Shoulder subluxation (x-ray)	Benefit of ES in reducing subluxation in acute hemiplegic subjects, but this benefit is not maintained once the stimulation course ends.

Author and year	*No. of subjects*	*Time after stroke*	*Exclusions*	*Randomi-sation method*	*Intervention(I) / Control (C)*	*Follow-up*	*Main outcome measures*	*Summary of findings*
Tekeoglu,1998 [172] 'Effect of transcutaneous electrical nerve stimulation (TENS) on Barthel Activities of Daily Living (ADL) index score following stroke'	60	30-240 days	Not stated	Block randomis-ation	I - 8 wks ES (to elbow and calf) for 0.5 hrs per day Mon-Fri i.e. total of 40 sessions C - sham treatment	8 weeks (i.e. after treatment) Blinded	- Barthel Index[92] - Modified Ashworth[156]	More dependent at baseline in the treatment group Improved ADLs in both groups, but more marked in treatment group and reached statistical significance. Significantly decreased spasticity in both groups.
Hesse, 1998 [173] 'Botox type A and short-term ES in the Rx of UL flexor spasticity after stroke :a randomized, double-blind placebo-controlled trial'	24 with severe upper limb flexor spasticity	Between 6 and 11 months (mean 7.45 months)	Contracture, previous treatment with botox, neurolytic or surgical procedures in affected limb, cognitive problems	Not known	I - Botox to biceps, brachialis and finger flexors ES to arm and forearm (30 minutes 3x/day for the 3 days after the injection C – no sham 4 groups (BT+ES, BT+ placebo, placebo, ES+ placebo)	Blinded 2, 6, 12 weeks after treatment	- muscle tone (Modified Ashworth[156]) - limb position at rest - difficulties encountered by patient/observed by caregiver with 3 ADLs	Authors conclude benefit of ES + botox. But spasticity results not significant. The only statistically significant result is seen with hand washing.

1.6.6.6 Published reviews of the RCTs

A number of published systematic reviews and meta-analysis of the randomised trials suggest that the evidence regarding the effectiveness of ES to the upper limb following acute stroke remains inconclusive (Table 4). None of these papers are re-analysis of primary data. The search strategy is detailed in Appendix 3.1.

The meta-analysis published by Glanz et al in 1996[4] looked at 4 RCTs. They commented that there was inadequate documentation of the randomisation process and/or blinding in these trials. The trials looked at ES to different joints (2 ankle[174, 175],1 knee[176], and 1 wrist[143]) and the data from both upper limb and lower limb joints is combined in this meta-analysis. They concluded that ES appears to improve muscle strength recovery after stroke but it was unclear whether this reflected a clinical benefit as well. They recommended that future studies should be blinded and sham-controlled.

In 1997, Binder-MacLeod et al published a review paper of FES[139]. They gave a historical overview of FES and its applications and then described studies that looked at its clinical efficacy in both the upper and lower limbs. They concluded that although studies had suggested that FES may have the potential for improving the gait of hemiplegic patients and for reducing shoulder subluxation in such patients, further clinical studies were needed. The authors stated that they felt that FES might become a more common clinical tool in the treatment of the hemiplegic patient in the future.

Chae and Yu published a critical review in 2000 of neuromuscular electrical stimulation in hemiplegia[177]. They reviewed the efficacy of NMES in facilitating post-stroke motor re-learning and in reducing shoulder subluxation and pain. They then reviewed the development of upper and lower extremity neuroprostheses and their efficacy in reducing physical impairment and disability.

Six trials of cyclic NMES for motor relearning were identified, 3 upper limb[152, 154, 155] and 3 lower limb[151, 174, 175] trials. All of the 6 studies had small sample sizes. In the upper limb studies, all reported improved outcomes in motor impairment with the NMES treatment. However, in the studies by Powell and Sonde, there was no sham treatment for the control group, and the groups had unequal treatment intensities. It is thus difficult to say whether benefits seen in these studies were from the NMES or from increased treatment intensity, and placebo effects could not be ruled out in the absence of a sham treatment. Only the study by Powell reported number of patients screened. In Chae's study, there was a

significant drop-out rate and the authors failed to use an intention-to-treat analysis. All of the upper limb studies evaluated disability, but only the study by Powell showed benefit with NMES, however this was not maintained after the treatment was stopped. Five controlled trials of EMG-stim or PFST for motor relearning were identified, 3 upper limb[143, 158, 178] and 2 lower limb[176, 179] trials. Of the 3 upper limb studies, one used matched controls (i.e. it did not use a randomised controlled design[178]). Again, the studies were reported as showing positive effects of stimulation on motor impairment but there were numerous flaws in study design. No longer term follow up was undertaken in either of the upper limb randomised trials[143, 158] and sample sizes were small in all of the studies. None of the 3 upper limb studies had a sham treatment for controls, and Bowman's study did not report their randomisation method.

Despite all of these limitations to the above studies, the authors of this review concluded that the evidence suggested that NMES enhances motor relearning in hemiplegia. They did, however, propose that future studies should be large, multi-centre, placebo-controlled, randomised clinical trials. They stressed that the studies should clearly define the study population and described the total number of patients screened in order to enable generalisability of findings. They stated the importance of identifying optimal stimulation parameters, and also suggested that stimulation techniques should be refined to maximise compliance and clinical outcomes.

This critical review then discussed 4 randomised trials of NMES for shoulder dysfunction in hemiplegia[82, 133, 138, 170]. Baker and Parker evaluated the NMES as a treatment, Linn as prevention, and Faghri evaluated it for both treatment and prevention. All studies demonstrated a reduction in shoulder subluxation, at least in the short term, but the effects on pain were inconsistent. There were methodical differences between studies. Chantraine's was the largest study but not all subjects had hemiplegia secondary to stroke. In addition, this study was not randomised, did not provide adequate baseline data, and was not blinded. Although Faghri's study looked at both treatment and prevention, shoulder pain and subluxation were not inclusion criteria. Linn's study showed a trend towards the benefit of NMES which was not statistically significant. The authors of the review hypothesised that this may have been because of small numbers, or inadequate stimulation dosing.

Again, the authors concluded that future studies were needed to address the methodological limitations of previous studies. The final section of this review discussed NMES as a motor neuroprosthesis in hemiplegia which will not be discussed in detail here.

A review in 2001 by Burridge et al[135] described in detail the theories behind motor re-learning following acute stroke and the evidence for the effect of ES on this re-learning process. They described the review by Chae and Yu in 2000 and commented on the methodological flaws in many of the published studies prior to the year 2000. The trials by Sonde, Chae and Powell[152, 154, 155] were then discussed in detail as their methodology was more 'robust'. The conclusions of these studies were that motor control improved with stimulation, but the authors of this review made the points that benefits were not sustained after treatment was discontinued, and that a reduction in impairment did not translate into an improvement in everyday activities. Finally, the use of EMG-triggered stimulation was discussed. The authors felt that putting the stimulation under the control of the patient may have been a more effective way (compared with cyclic ES) of improving motor re-learning, especially if the movement produced was a task-orientated one. They described 2 studies[158, 178] which showed positive results.

The authors concluded that ES would be widely used in the future but that there needed to be an improved understanding its interaction with the central nervous system, and sound clinical evidence for its effectiveness. The authors concluded that, in order to achieve these goals, further trials were needed. These trials must be large, randomised and controlled, using rigorous methodology, and appropriate outcome measures.

In 2001, a Cochrane review of electrical stimulation to the upper limb after stroke found significant benefits for range of pain-free humeral lateral rotation and glenohumeral subluxation[5]. There was no improvement in patients' reports of shoulder pain, although this may have been due to inconsistencies in the use of pain rating scales by stroke patients[129]. There was no overall improvement in upper limb function, although significant benefit was reported from two of the four studies included in the meta-analysis[82, 155]. It was uncertain whether the overall effect on recovery did not reach statistical significance because of the absence of any true benefit, or whether this was due to the large variation in study design and outcome measures used, and small numbers of study participants. The largest trial which investigated the effects of electrical stimulation on upper limb recovery found an impressive beneficial effect, but was not included in the analysis as a small percentage of study subjects had hemiparesis due to head injury rather than stroke[170]. The Cochrane Review concluded that there was an urgent need for adequately sized randomised controlled trials to investigate the effects of electrical stimulation on upper limb recovery and shoulder pain after stroke.

Chae and Yu published a further review of ES in 2002[180]. This reviewed the same literature as the review of 2000, except that the study by Cauraugh[88] was added to the section about the use of EMG-stim for motor relearning in hemiplegia. The conclusions drawn were as already discussed and the need for future trials was again stated. There was more detail in this paper regarding refining electrical stimulation techniques i.e. the use of percutaneous ES rather than surface ES.

A review by Yu and Chae, also published in 2002[181], discussed ES specifically for shoulder dysfunction. The studies by Baker, Faghri, Chantraine, and Linn[82, 133, 138, 170] were discussed. In addition, studies by Kobayashi and Wang[169, 171] were reviewed. The authors again reported in detail the methodical limitations of all of the studies, but concluded that ES reduces subluxation and may improve shoulder range of motion, enhance upper limb motor recovery, and reduce pain. The rest of the review discussed intramuscular NMES as an alternative therapy that is less painful and easier to apply than sNMES[182]. They reported a pilot study to investigate the effects of intramuscular NMES[183] which demonstrated its feasibility although they acknowledged that further research was needed to evaluate its efficacy.

A meta-analysis was undertaken by Ada et al in 2002[184]. The primary purpose of this was to examine the efficacy of surface ES, which produced a motor response in supraspinatus and posterior deltoid, in both preventing and reducing subluxation at the shoulder. The secondary purpose was to examine the efficacy of surface ES in improving function of the shoulder both early (defined as within 2 months) or late (more than 2 months) after stroke.

They reviewed the trials by Baker, Faghri, Kobayashi, Linn and Wang[82, 133, 138, 169], all of which looked at ES to supraspinatus and posterior deltoid as an adjunct to conventional therapy. The methodological quality of each was assessed using the PEDro scale[185]. They noted that the methods of assessing outcomes were similar for subluxation but more varied for function and pain.

By pooling data from these trials, they stated that early ES plus conventional therapy was superior in reducing subluxation to conventional therapy alone. This was not the case for late ES however. In order to compare the effect of ES on function, outcome scores were converted to a percentage, and a random effects model used. This enabled pooling of this data and the results showed that early (but not late) ES was beneficial. In preventing pain (measured using a goniometer), there was no evidence that early ES was beneficial, but late ES may have been.

In summary, they concluded that there was evidence to support the efficacy of early ES (as an adjunct to conventional therapy) for preventing shoulder subluxation and for increasing upper limb function, and of late ES in reducing pain. They therefore recommended that stroke patients with a score of less than 4 on item 6 of the MAS[102] early after stroke should receive ES to the shoulder. They acknowledged that their findings with regard to subluxation were similar to those stated in the Cochrane review[5] but that their results regarding pain were conflicting with this review. They suggested that this may be because the Cochrane review included trials where ES produced a sensory response as well as a motor one. They also pointed out that the trial by Wang et al[171] had unusually small standard deviations, and if this trial was removed from the meta-analysis, there was no evidence of a beneficial effect of ES on function (in keeping with the Cochrane review).

A systematic review of TES was undertaken by de Kroon and colleagues in 2002[62]. Their objective was to assess the available evidence on the effect of TES of the affected upper extremity in improving motor control and functional abilities after stroke. They focussed specifically on TES rather than FES and identified 6 RCTs which met their criteria for selection. All of these trials looked at ES of the arm and wrist and 3 looked at patients in the acute phase after stroke[152, 154, 158]. There were large differences between the trials in terms of time to randomisation, ES regime used and outcome measures. All of the studies looked at motor recovery but only 2 actually assessed functional abilities[88, 152]. In two of the studies, a post-hoc subgroup analysis was undertaken to compare those less severely affected with those more severely affected. One study reported a significantly better effect on motor control in the less severely affected group than the more severely affected [155], and the other reported a significant effect on functional abilities in the less severely affected group but no effect in the whole group [152]. De Kroon and colleagues concluded that there was evidence for a probable positive effect of TES on motor recovery, but none yet for a beneficial effect on function.

A further review by Chae in 2003[186] looked at the same studies as were discussed in 2002[181] and there was again detail regarding intramuscular ES as described above.

Handy et al undertook a meta-analysis in 2003[187]. The purpose was to examine the effectiveness of ES for stroke patients in reducing shoulder subluxation, increasing range of motion of the shoulder, reducing pain, and improving functional use of the upper extremity. They recognised the paucity of RCTs of treatment and prevention of shoulder pain in stroke patients, and acknowledged that the measurement of pain is subjective. They reviewed the studies by Chantraine, Faghri, Cauraugh, Wang and Linn[82, 133, 170, 171, 188]. They concluded

that there was evidence that ES produced a beneficial effect on range of motion, pain, upper extremity function, and subluxation, but acknowledged that their meta-analysis was limited by the small number of studies.

A further meta-analysis by Bolton et al in 2004[189] assessed the effect of EMG-triggered neuromuscular stimulation on hand and arm function. They acknowledged that the different performance outcomes made it difficult to pool multiple studies for a robust comparison. In this meta-analysis, outcomes were looked at in terms of function and impairment. They looked at studies by Kraft, Hummelsheim, Francisco, Cauraugh, and Cauraugh & Kim[88, 158, 178, 188, 190]. It is important to note that the studies by Kraft and by Hummelsheim were not randomised controlled trials.

A large mean effect size was seen when pooling data from these studies which indicated a significantly positive influence of EMG-triggered NMES on motor recovery outcome measures. However, the authors acknowledged that the quality of the 5 studies was variable but they chose to include them all as there were so few.

Table 4: Review Articles of ES

Author and year	***Review type***	***Clinical articles reviewed (upper limb ES)***	***Conclusions***	***Comments***
Glanz et al 1996[4] 'Functional Electrostimulation in Poststroke Rehabilitation: A Meta-Analysis of the Randomised Controlled Trials'	Meta-analysis	Bowman et al 1979[143]	Efficacy of FES in improving muscle strength after stroke but this does not necessarily translate into a clinical benefit. Does not address question of sustained treatment effects for FES after it is discontinued. Future studies should be double-blind and sham-controlled.	Combines data from joints in upper limb and lower limb extremities. (1 upper limb and 3 lower limb studies)
Binder-MacLeod 1997[139] 'Assessment of the Efficacy of Functional Electrical Stimulation in Patients with Hemiplegia'	Review	Stanic et al 1978[191] Takebe et al 1975[192] Waters et al 1975[193] Kralj et al 1977[146, 147] Rebersek et al 1973[145] Baker et al 1979[194] Bowman et al 1979[143] Baker 1986[138] Faghri et al 1994[82]	FES may have the potential for improving the gait pattern of hemiplegic patients and for reducing subluxation. Additional clinical studies needed. Controlled studies showing successful treatment of the hemiplegic hand were not currently available. FES may become a more common clinical tool in the treatment of the hemiplegic patient in future.	Historical and clinical review
Chae and Yu 2000[177] ' A critical review of neuromuscular electrical stimulation for treatment of motor dysfunction in hemiplegia'	Review	Sonde et al 1998[155] Chae et al 1998[154] Powell et al 1999[152] Bowman et al 1979[143] Francisco et al 1998[158] Kraft 1992[178] Baker 1986[138] Chantraine 1999 [170] Linn et al 1999[133] Faghri et al 1994[82]	Some evidence suggesting that NMES enhances motor relearning in hemiplegia, and can prevent/treat shoulder subluxation and pain, but many methodological limitations. Future studies must address these limitations.	Similar reviews in 2002 and 2003

Author and year	***Review type***	***Clinical articles reviewed (upper limb ES)***	***Conclusions***	***Comments***
Burridge et al 2001[135] 'Clinical and therapeutic applications of neuromuscular stimulation: a review of current use and speculation into future developments'	Review	Sonde et al 1998[155] Chae et al 1998[154] Powell et al 1999[152] Kraft 1992[178] Francisco et al 1998[158]	Evidence that motor control is improved with stimulation, but benefits not sustained after treatment discontinued, and reduction in impairment did not translate into improvement in everyday activities. EMG-stim may be a more effective way of improving motor re-learning, especially if the movement produced is a task-orientated one. There needs to be an improved understanding of the way ES interacts with the central nervous system, and also needs to be sound clinical evidence for the effect of ES.	3 trials of cyclic ES; 2 trials of EMG-stim
Price 2001[5] 'Electrical Stimulation for preventing and treating post-stroke shoulder pain: a systematic Cochrane review'	Systematic review	Faghri et al 1994[82] Leandri et al 1990[132] Linn et al 1999[133] Sonde et al 1998[155]	Currently no evidence to confirm or refute that ES can influence reports of shoulder pain after stroke. There is a need for adequately powered RCTs to examine the role of ES for prevention of shoulder pain in acute stroke patients.	All trials of ES to the shoulder
Chae and Yu 2002[180] ' Neuromuscular electrical stimulation for motor restoration in hemiparesis'	Review	Sonde et al 1998[155] Chae et al 1998[154] Powell et al 1999[152] Bowman et al 1979[143] Francisco et al 1998[158] Kraft 1992[178] Baker 1986[138] Chantraine 1999[170] Linn et al 1999[133] Faghri et al 1994[82] Cauraugh et al 2000[88]	See review in 2000 (discussed above). More detail in this paper regarding refining ES techniques i.e. the use of percutaneous rather than surface ES.	The study by Kraft was not an RCT

Author and year	*Review type*	*Clinical articles reviewed (upper limb ES)*	*Conclusions*	*Comments*
Yu and Chae 2002[181] ' Neuromuscular stimulation for treating shoulder dysfunction in hemiplegia'	Review	Baker 1986[138] Faghri et al 1994[82] Chantraine 1999[170] Linn et al 1999[133] Kobayashi et al 1999[169] Wang et al 2000[171]	Methodological limitations of studies acknowledged. There is evidence that ES reduces shoulder subluxation and may improve shoulder range of motion, enhance upper limb motor recovery and reduce pain.	All trials of ES to shoulder
Ada et al 2002[184] ' Efficacy of electrical stimulation in preventing or reducing subluxation of the shoulder after stroke: a meta-analysis'	Meta-analysis	Baker 1986[138] Faghri et al 1994[82] Kobayashi et al 1999[169] Linn et al 1999[133] Wang et al 2000[171]	Early ES plus conventional therapy is superior in reducing subluxation and increasing upper limb function than conventional therapy alone. Evidence that late ES is superior in reducing pain	
de Kroon 2002[62] 'Therapeutic electrical stimulation to improve motor control and functional abilities of the upper extremity after stroke: a systematic review'	Systematic review	Powell et al 1999[152] Chae et al 1998[154] Sonde et al 1998[155] (and 2000[157]) Francisco et al 1998[158] Bowman et al 1979[143] Cauraugh et al 2000[88]	Suggests a positive effect of ES on motor control of the affected upper extremity after stroke but not known whether this improvement is clinically relevant or whether functional improvement can be achieved by ES.	All upper limb ES trials (wrist and fingers only, none of ES to the shoulder). Not possible to draw conclusions regarding function in this review as this was only addressed by 2 out of the 6 studies.
Chae 2003[186] ' Neuromuscular electrical stimulation for motor relearning in hemiparesis'	Review	Baker 1986[138] Faghri et al 1994[82] Chantraine 1999[170] Linn et al 1999[133] Kobayashi et al 1999[169] Wang et al 2000[171]	See review by Yu and Chae in 2002	

Author and year	*Review type*	*Clinical articles reviewed (upper limb ES)*	*Conclusions*	*Comments*
Handy et al 2003 (187) ' Meta-analysis examining the effectiveness of electrical stimulation in improving functional use of the upper limb in stroke patients'	Meta-analysis	Chantraine 1999(170) Faghri et al 1994(82) Cauraugh et al 2000(88) Wang et al 2000(171) Linn et al 1999(133)	Evidence that ES has beneficial effects on range of motion, pain, upper extremity function and subluxation. But meta-analysis was limited by the small number of studies.	
Bolton et al 2004(189) 'Electromyogram-triggered neuromuscular stimulation and stroke motor recovery of arm/hand functions: a meta-analysis'	Meta-analysis	Kraft 1992(178) Hummelscheim et al 1997(190) Francisco et al 1998(158) Cauraugh et al 2000(88) Cauraugh and Kim 2003(24)	Evidence of a significantly positive influence of EMG-stim on motor recovery outcome measures. But the methodological quality of the studies was variable.	The studies by Kraft and Hummelscheim were not RCTs

1.7 Summary of introduction

- Upper limb impairment affects the majority of stroke survivors, and over half of these still experience problems 6 months later.
- The effectiveness of many upper limb rehabilitation interventions is unclear.
- A variety of scales are available for measuring outcome in upper limb rehabilitation and it is important that ones chosen are valid, reliable, and relevant to the intervention and study population.
- Electrical stimulation (ES) has been proposed as a safe method of improving outcome after stroke but the evidence for its effectiveness is unclear. The literature suggests that ES is effective in reducing subluxation following stroke and may have a beneficial effect on upper limb impairment and pain. However, the evidence is lacking that this is translated into clinical benefit i.e. an improvement in upper limb function and pain.
- Previous studies of ES to the upper limb following stroke have methodological limitations. Many have recruited small numbers of subjects, have failed to use a secure randomisation method, have not used sham treatments for controls and/or have not used blinded, validated and reliable outcome measures. The setting for these studies has not always been in stroke units.
- It is currently unclear what an ES programme should include (i.e. the amount and intensity of stimulation).
- Reviews of the literature have suggested that there is a need for larger, randomised controlled trials with robust methodology.
- Studies have suggested that subjects with a greater severity of upper limb weakness gain more benefit from ES treatment. However, evidence of benefit for other subgroups is lacking, so subjects with all levels of upper limb impairment should be included in future studies.

Chapter 2 Aims and Objectives

2.1 Aim

To evaluate a four week programme of surface neuromuscular electrical stimulation (sNMES) for subjects with upper limb impairment following acute stroke.

2.2 Objectives

- To compare the upper limb function and impairment of stroke subjects who receive a programme of surface neuromuscular electrical stimulation (sNMES) to the upper limb (the intervention group) with those receiving placebo (the control group) at the end of a four week intervention period and three months after stroke.
- To compare the prevalence of post-stroke upper limb pain between the intervention and control group at the end of a four week intervention period and three months after stroke.
- To compare disability and global health status of the intervention and control group at three months after stroke.
- To seek the experiences and views of subjects about sNMES.

Stroke patients wish to regain useful upper limb movement, so the primary outcome measure chosen for this study was upper limb function. Previous studies have looked at the effect of ES on subluxation, motor recovery and pain, and although there is evidence of the beneficial effect of ES on these, it is not clear whether this translates into improved functional recovery. The timings of assessments were chosen to coincide with the end of the treatment period and to look at longer term effects. Three and six months are widely used time points for measuring outcomes in stroke research. Three months was selected to enable comparisons with other studies, and to enable the research to be undertaken within the timescale available for an MD thesis.

Although there is evidence that ES is beneficial in improving joint alignment (i.e. reducing or preventing subluxation) and reducing spasticity)[5, 62], these outcomes were not measured in this study. There is often confusion when trying to define subluxation[33], and its

measurement is unreliable and often of no new clinical significance[181]. There is no validated measure of upper limb spasticity other than at the elbow[156].

At the 3-month assessment, participants were asked whether or not they had experienced symptoms from the ES, and to give their views on which stimulator they thought they had received.

There was one pre-planned subgroup analysis in this study. This was to look at the outcomes of participants with mild/moderate upper limb function (ARAT>0) and those with severe functional impairment (ARAT=0) at the initial assessment. There is evidence that the severity of initial upper limb motor impairment is a predictor of upper limb recovery[3, 65], and there is also some evidence that ES is more beneficial in stroke patients with a milder degree of upper limb impairment[155].

Some of the outcome assessments were undertaken immediately after the intervention period and at 3 months (i.e. measures of impairment, function and pain), whereas others (disability and global health status) were only undertaken at 3 months. This was because outcomes such as impairment and pain were expected to be affected early after treatment whereas disability would be later effect. The difference in timings of outcome assessments therefore reflects this. A number of study participants were also likely to still be in hospital at the 4-week assessment so measurement of E-ADLs would not be possible.

2.3 Compliance with treatment

Previous studies of electrical stimulation have described the participants' intended amount of stimulation but only two[152, 167] reported the amount of stimulation actually received. In a RCT, the treatment received by randomisation groups should differ only in receipt of the intervention. In this study, the amount of sNMES or sham given was recorded by the use of diaries (Chapter 6).

2.4 Inter-observer study

We undertook an inter-observer study to look at the inter-observer reliability of our outcome measures. We wanted to ensure that there was good reliability, i.e. minimal inter-observer variability, between the 2 nurses undertaking the blinded outcome assessments, and between the research fellow (CC) undertaking the initial assessments and these nurses (Chapter 7).

Chapter 3 Methods

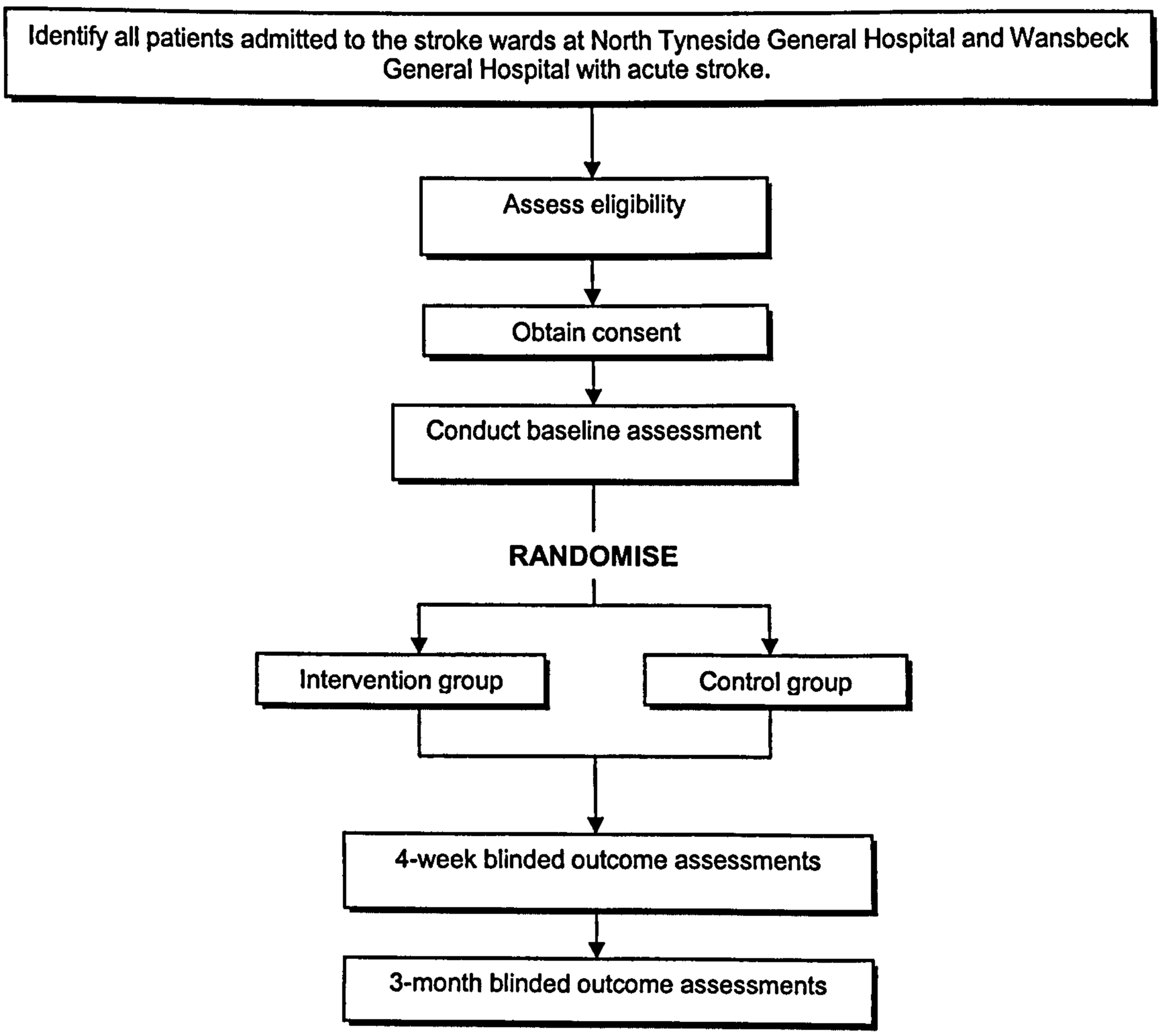
3.1 Design

A two-centre pragmatic randomised controlled trial

3.2 Study Design

The design of the study is shown in Figure 1.

Figure 1: Study Design



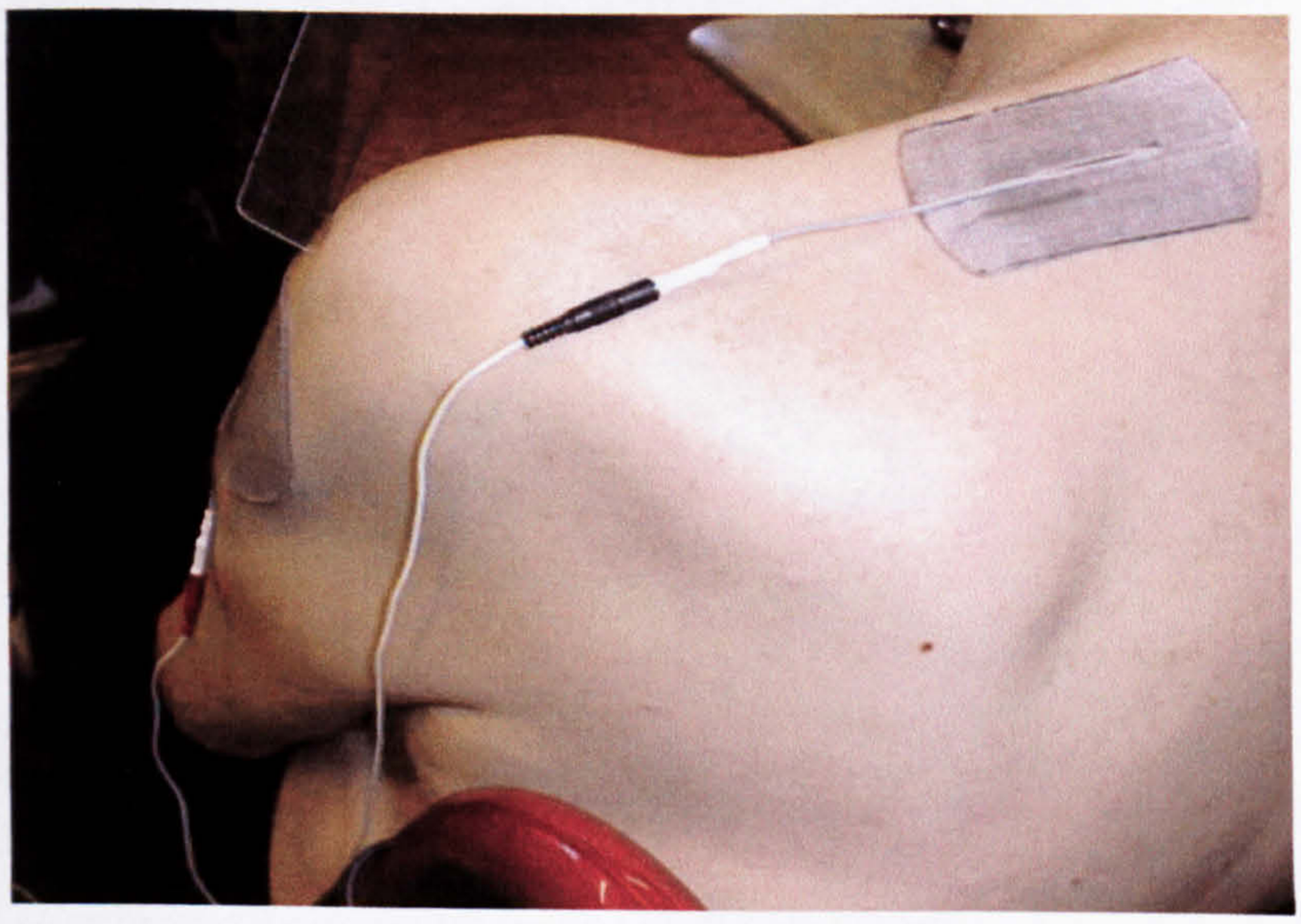
The study design was in place prior to the appointment of the research fellow (CC). An application for a Teaching and Research Fellowship was made to Northumbria Healthcare NHS Trust in order for the study to be undertaken. This application was accepted and CC was appointed this post to start on 1st November 2001.

The research fellow (CC) wrote applications for ethical and Trust approval, wrote applications for funding to Remedi (successful) and PPP Healthcare (unsuccessful), designed study protocols for the day-to-day running of the project, developed assessment questionnaires, organised training in the delivery of sNMES, and held launch meetings for clinical staff before recruitment commenced.

3.3 Intervention

This comprised a standard programme of surface neuromuscular electrical stimulation (sNMES) to the upper limb commencing within 10 days of stroke onset. The following regimen was chosen as it has been used in previous trials and is widely used in clinical practice. Two surface electrodes placed over supraspinatus and posterior deltoid on the stroke affected side were used (Figure 2).

Figure 2: Positioning of electrodes



The basic stimulation frequency was 30 Hz. The stimulator on time and the stimulator off time were 15 seconds with a 3 seconds ramp up and 3 seconds ramp down time. The intervention group received a level of stimulation that was increased until a comfortable visible contraction of the shoulder muscles was clearly seen during each "on" period.

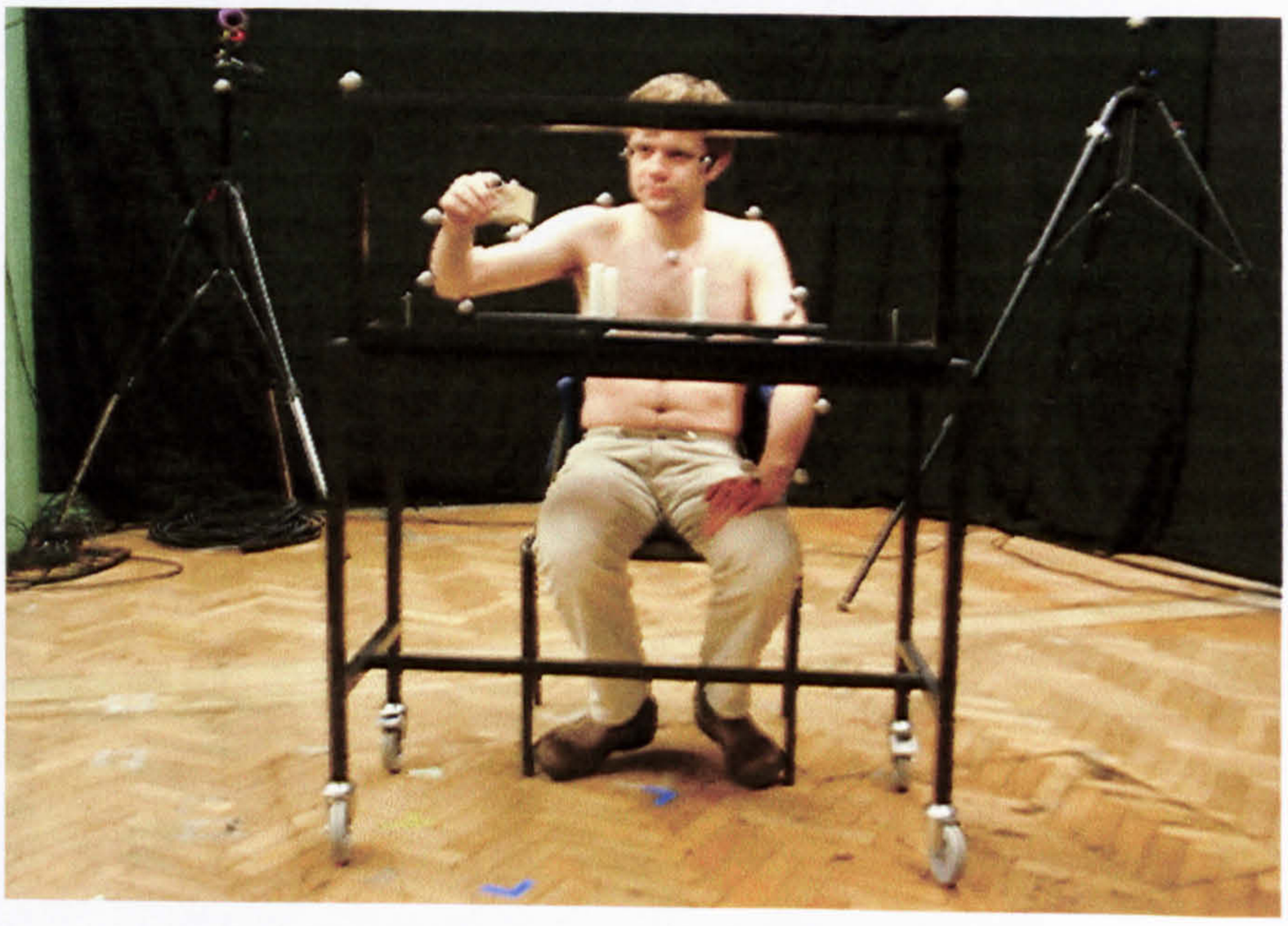
The 'sham' stimulator was identical to this intervention stimulator but an internal disconnection prevented any current from being delivered. It was applied in the same way, and the settings adjusted to a mid-point.

In addition to their other rehabilitation needs, participants received a four-week programme of sNMES which was delivered outwith their individualised therapy sessions. On the first day participants received 30 minutes of sNMES and the duration of treatment was increased over the first week according to a study protocol until 3 x 1 hour treatment sessions per day were achieved, which was then administered daily for the next three weeks. Stroke unit therapists and nursing staff were trained in the technique so that it could be delivered seven days per week. Where possible, participants who left hospital before the end of the four-week intervention period continued to receive sNMES in their own homes. Training was given to participants, carers and support workers to enable them to use the equipment and members of the study team were available to deal with any queries or issues that arose.

3.4 Primary outcome measure

- Upper limb function - Action Research Arm Test (ARAT)[6, 7] at 3 months after stroke (Figure 3). This was chosen because it is a robust test, with proven validity and reliability in stroke patients, which assesses different components of arm function.

Figure 3: Action Research Arm Test



3.5 Secondary outcome measures

These were undertaken at the end of the four-week intervention period and three months after stroke.

- Upper limb pain - 5-point severity scale and 0-10 numerical rating scale[127, 128]
- Pain free range of humeral lateral rotation[130, 131] (degrees).
- Impairment – Motricity Index[9]; Star Cancellation Test of visuospatial impairment[79, 80]
- Upper limb function – ARAT (4 weeks)[6, 7]; Frenchay Arm Test (FAT)[8]
- Disability – Nottingham Extended Activities of Daily Living (E-ADL) Index (3 months only)[110]
- Global health status – Nottingham Health Profile (NHP) (3 months only)[116]
- Experience and views of participants about sNMES – patients were asked which stimulator they thought they had received. They were also asked to comment on whether or not they had experienced symptoms from the sNMES, and were asked in general how they found the stimulator.

3.6 Calculation of sample size

A difference of 8 points on the ARAT score[6, 7] was defined as clinically significant. This difference of 8 represented an improvement of 2 points on all 4 subtests of the ARAT[6, 7]. In practice, this is the difference between not being able to do a subtest and then to partially complete it, or being able to partially do a subtest and then complete it fully. This clinical definition has not been used in previous studies. Using variance and effect size from previous studies we initially calculated that 180 subjects were needed to achieve a 90% chance (power 0.9) of detecting this 8 point difference (0.25 standard deviations) between mean ARAT[6, 7] scores in the intervention group and the control group (two tailed alpha =0.05). This sample size would also produce a 90% chance (power 0.9) of detecting a 0.5 point difference (0.54 standard deviations) between mean FAT scores[8] (two tailed alpha =0.05). Allowing for 9% attrition of subjects (as experienced in previous studies) we planned to recruit 198 subjects. Eight hundred acute stroke patients are admitted to North Tyneside (NTGH) and Wansbeck General Hospitals (WGH) each year. Using the stroke register we estimated that 12 patients per month would be eligible to participate and that recruitment would be complete in 17 months.

Recalculation of power was undertaken at the end of December 2002 as recruitment rates were lower than predicted. To give an 80% chance (power 0.8) of detecting the above differences in mean ARAT[6, 7] and FAT scores[8], taking into account our actual attrition rate of 8%, we calculated that we would need to recruit a total of 168 patients.

3.7 Ethical and Trust approval

Permission to carry out the study was obtained from Newcastle and North Tyneside Joint Ethics Committee, Northumberland Ethics Committee (Appendix 2.1) and Northumbria Healthcare NHS Trust. The project was registered in accordance with the Data Protection Act.

North Tyneside and Wansbeck are district general hospitals within Northumbria Healthcare NHS Trust. Approximately 800 patients with acute stroke are admitted to these 2 hospitals each year. Patient populations and stroke management at these 2 sites are typical of hospitals throughout the UK. Both hospitals have an acute stroke unit. NTGH has a stroke rehabilitation ward on the acute hospital site. Stroke patients at WGH are rehabilitated initially on the acute stroke ward, and then transferred to one of 4 community hospitals (based at Morpeth, Blyth, Alnwick and Berwick) for further stroke rehabilitation.

3.8 Case ascertainment

All patients admitted to the stroke wards at NTGH and WGH were identified by regular (twice weekly at each site) contact with the wards.

3.9 Eligibility criteria

All patients admitted to the stroke wards at NTGH and WGH within 10 days of acute stroke were assessed against the following eligibility criteria:

Residence

- Usual residence in North Tyneside (NTGH patients) or in the catchment area for Morpeth Cottage Hospital (or Blyth Cottage Hospital from 1/7/02) (WGH patients).

Patients living in the catchment area for Berwick and Alnwick Infirmary were excluded for logistical reasons.

Pre-morbid features

- No other diagnosis likely to significantly interfere with rehabilitation.
- Pre-stroke Oxford Handicap Scale[195] score < 4.
- No previous major upper limb problem (stroke-affected side) likely to influence assessments i.e. an upper limb amputation/atresia, significant upper limb impairment from previous stroke, diagnosis of frozen shoulder, dislocation or fracture of the upper limb within 1 month.
- No regular analgesia specifically for the upper limb (stroke-affected side).
- No reason to preclude electrical stimulation (e.g. the presence of a permanent pacemaker or implantable defibrillator, a history of previous life-threatening cardiac arrhythmias, the presence of a metallic shoulder implantation on the stroke-affected side).

Clinical

- Medically stable.
- Patient opens eyes spontaneously or to speech (i.e. Glasgow Coma Scale[196] > 4).
- No cognitive or language impairment likely to influence assessments
- Evidence of upper limb weakness/drift and/or finger-nose incoordination and/or star cancellation fail.

Reasons for non-eligibility were recorded on a standard proforma.

We aimed to recruit patients with a wide range of upper limb impairments. All participants were required to have evidence of upper limb weakness/drift and/or finger-nose in-coordination and/or visual inattention. There is a wide variation in professionals' views as to who should be given sNMES and, in clinical practice, it is given to patients with a range of deficits. We also recruited patients with different stroke subtypes as there is no rationale to believe that stroke subtype (i.e. the vascular territory affected) can determine the effects of sNMES.

3.10 Assessment of eligibility

Patients on the stroke wards were screened by a ward doctor using the eligibility criteria (Appendices 2.2 and 2.3). All eligible subjects were given a patient information leaflet (Appendix 2.4). The research fellow (CC) checked the names of those subjects screened against the names in the ward admission book to ensure that all new stroke admissions had been screened (Appendix 2.5).

3.11 Consent

The research fellow (CC) discussed the study with all eligible subjects to ensure that they had had time to consider the contents of the information sheet and that it had been clearly understood. The research fellow (CC) also answered any questions and confirmed eligibility prior to seeking written consent (Appendix 2.6).

3.12 Initial assessment

This was undertaken by the research fellow (CC) for all eligible subjects who had given written consent (Appendix 2.7). It consisted of demographic details, handedness, other relevant co-morbidity, new neurological impairment[197], stroke subtype[198], and the CT head scan result.

The research fellow then completed the following assessments for each participant:

- Oxford Handicap Scale (OHS)[195]
- Pain scale (pre and post-stroke)[127, 128]
- Nottingham E-ADL Index (pre-stroke)[110]
- Abbreviated Mental Test Score[159]
- Sheffield Aphasia Screening Test for acquired language disorders[199]
- *Motricity Index[9]
- *Frenchay Arm Test (FAT)[8]
- *Action Research Arm Test (ARAT)[6, 7]
- Shoulder Shrug Test[71]
- National Institute of Health Stroke Scale[197]
- *Star Cancellation Test[79, 80]

- Measurement of passive and active range of pain-free humeral external rotation[130, 131]
- Basic testing of sharp-dull and hot-cold discrimination (to identify subjects at risk of central post-stroke pain in the upper limb)[200]
- Measurement of upper arm girth[133]

*Inability to perform these assessments was scored as zero.

The completed initial assessment forms were returned to the project secretary for entry onto a database designed specifically for the study. An information letter was sent out to the participant's general practitioner when the initial assessment details were entered onto the database (Appendices 2.8 and 2.9).

3.13 Seven-day assessment

At seven days after stroke, nursing staff were asked to complete the Barthel Activities of Daily Living (ADL) Index[92] to measure disability (Appendix 2.10).

3.14 Randomisation

All eligible subjects were randomised using a central independent telephone computerised service based at the University of Newcastle upon Tyne. Participants were stratified by severity of upper limb weakness according to the FAT[8] (scores 0,1 vs. scores 2-5). Participants were randomised to either the intervention or control group. There were no crossovers between groups.

All of the sNMES boxes had a serial number inside the battery compartment. All the boxes were also labelled on the outside with another number (1, 2, 3 etc.) which was known as the 'box number'. A list was kept at the University detailing each box (its box number and serial number), whether it was intervention or placebo and whether it was located at NTGH or WGH.

The research fellow (CC) telephoned the database manager who entered the name, FAT score[8] and subject location (NTGH or WGH) onto a database which was set up to randomly allocate participants to either the intervention group or the control group in blocks of eight, i.e. for every eight subjects entered into the study, four were in the intervention group and four were in the control group.

Once the participant had been randomised, the database manager informed the research fellow (CC) of the randomisation group, participant study number and box number. The research fellow (CC) recorded this box number and study number in the participant's stroke pathway, and collected this box from the ward. The randomisation group was not recorded. A blank white sticker was used to label the box with the participant's name and date of birth. A yellow sticker (Appendix 2.11) was placed on the inside back cover of their medical notes to clearly indicate that they were participating in the study.

The research fellow (CC) then prescribed the sNMES on the participant's drug kardex. The research fellow (CC) set up the sNMES equipment on the participant with a member of stroke unit staff to ensure that it was done correctly. The sNMES was then commenced according to the study protocol.

3.15 Applying and using sNMES

Training was given to specific stroke unit nurses in applying and using the sNMES equipment (Appendix 2.12).

The two sites for the electrodes were supraspinatus and deltoid on the stroke-affected upper limb. These sites were marked on the arm with a waterproof pen to aid future treatment sessions prior to putting the electrodes in position. The wires were then attached to the electrodes (red to the top electrode, black to the bottom) and to the box. Initially, the box mode was set to 'continuous' (mode 2) before setting the intensity level.

The intensity knob was turned up slowly until muscle movement was seen at the shoulder. Once muscle movement was seen, the intensity knob was not turned up any further and the intensity level was noted. It was turned up slowly to enable subjects to become accustomed to any symptoms that they might experience, and to ensure that the level was not set higher than that required to produce movement at the shoulder. The intensity level remained approximately the same throughout treatment sessions. In the placebo group, the equipment was identical to that of the intervention group but an internal disconnection prevented any current from being delivered. In this case, no shoulder movement was seen and the intensity level was set at level 5.

The box mode was then changed directly over to 'alternate' (i.e. to deliver an intermittent current) (mode 3) and the equipment left in place for the duration of the treatment session.

The protocol for the timing of the sNMES was the same in both the intervention group and the placebo/control group and is as follows:

Day 1	Half an hour twice daily (morning and evening)
Day 2	Half an hour twice daily (morning and evening)
Day 3	Half an hour three times daily (morning, lunch and evening)
Day 4	Half an hour three times daily (morning, lunch and evening)
Day 5	1 hour in the morning, 1 hour at lunchtime, half an hour in the evening
Day 6	1 hour in the morning, 1 hour at lunchtime, half an hour in the evening
Day 7 onwards	1 hour three times daily (morning, lunch and evening)

A timer was provided with each box which was used to time each session and was a reminder to stroke unit staff to turn off the equipment once the treatment session was complete.

If subjects were to be discharged within the four-week treatment period, the participant and/or relative/carer was trained to apply the sNMES prior to the participant's discharge so that the sNMES could continue at home.

At the start of the study, participants planned for discharge during the course of sNMES were asked to perform the ARAT[6, 7]. Those achieving a maximum score were discharged home without the sNMES. The primary outcome measure was the ARAT and it was therefore decided that those achieving a maximum score on this test pre-discharge were not required to continue the sNMES at home. However, it was not practical to perform a pre-discharge ARAT on all participants due to be discharged and so it was decided in July 2002 (6 months after the start of recruitment) to discharge all participants with the sNMES equipment unless there was another reason not to do so.

3.16 Recording sNMES

The research fellow (CC) prescribed the sNMES treatment sessions on the participant's drug kardex and stroke unit staff signed for this treatment each time it was given.

In addition, each participant was given a study diary (Appendix 2.13). The participant's name, study number, box number and sNMES intensity level were all documented in the diary by the research fellow (CC). The diary contained clear instructions for the timings of the sNMES treatment sessions as detailed above. For each treatment session, stroke unit staff ensured that participants were given the same sNMES box by checking that the box number corresponded to that recorded in the participant's diary.

The treatment sessions were recorded in the diary by documenting the start and finish times. The diary was also used to record reasons for non-receipt of treatment and for staff to record comments about any difficulties encountered.

Patients received a programme of therapy in addition to the sNMES sessions which was individualised and delivered by the multi-disciplinary team. We did not attempt to standardise the type and amount of therapy received as this would have been inappropriate. We believe that the amount and type of therapy received by patients is similar across sites; this was not formally recorded as it would have been difficult and time consuming to do accurately with the resources available.

3.17 Staff training and use of sNMES

Stroke unit staff at NTGH, WGH, Morpeth Cottage, and Blyth Community Hospitals were trained in applying and using sNMES. Newsletters were mailed out every 4 to 6 months to inform staff of the progress of the study (Appendix 2.14). Two lunchtime meetings were also held in each hospital during the first 6 months of the study to provide further training in the use of the sNMES equipment, and to answer any staff concerns or questions. The research fellow (CC) visited the wards on a weekly basis to ensure that the application of sNMES was correct, to provide individual staff training and to answer any questions.

3.18 Follow-up assessments

A research nurse who was "blind" to the randomisation group undertook follow-up assessments at the completion of the four-week sNMES programme (Appendix 2.15) and three months after stroke (Appendix 2.16). The research fellow trained the research nurses to perform the assessments prior to the start of the study. Assessments took place in the hospital if the participant was an in-patient or if the participant had been discharged but was well enough to travel and happy to do so. Transport was provided. Participants who did not wish to or who were unable to travel to hospital were assessed in their own home.

Before contacting the participant, the research nurse obtained the following details for each participant by reviewing the medical notes:

- Whether the participant was still alive
- Participant's date of death (if applicable)
- Whether the participant was discharged following their stroke
- Date of discharge (if applicable)
- Details of readmission to hospital (if applicable)
- Current contact address
- Current contact telephone number
- Details of any treatment interventions given for the upper limb (e.g. oral analgesia, steroid injection etc.)
- New medical problems or new upper limb problems.

3.18.1 Four-week assessments

The four-week assessment was undertaken after completion of the course of sNMES i.e. on day 29 (+ 7 days after this i.e. up to day 35) after randomisation. As participants were recruited within 10 days of stroke, this assessment was performed up to 45 days after stroke. It was a face to face interview and assessment of upper limb function by a blinded research nurse and consisted of the following:

- Pain scale[127, 128]
- Oxford Handicap Scale[195]
- Barthel ADL index[92]
- Star Cancellation Test[79, 80]
- Motricity Index[9]
- Shoulder Shrug Test[71]
- Frenchay Arm Test[8]

- Action Research Arm Test[6, 7]
- Measurement of humeral lateral rotation[130, 131] and upper arm girth[133]

Reasons for non-completion of the assessment were recorded. At the 4-week assessment, the diary was collected and the sNMES equipment returned to its original ward.

3.18.2 Three-month assessments

The three-month assessment was undertaken on day 90 (+/- 7 days before or after this i.e. between day 83 and 97) after stroke. It was a face to face interview and assessment of upper limb function by a blinded research nurse and consisted of the following:

- Pain scale[127, 128]
- Oxford Handicap Scale[195]
- Barthel ADL Index[92]
- Nottingham E-ADL Index[110]
- Star Cancellation Test[79, 80]
- Motricity Index[9]
- Shoulder Shrug Test[71]
- Frenchay Arm Test[8]
- Action Research Arm Test[6, 7]
- Measurement of humeral external rotation[130, 131] and upper arm girth[133]
- Participant's views regarding sNMES

In addition to the above, details of whether the participant was still receiving physiotherapy was recorded. Following the assessment, the participant was asked to complete the Nottingham Health Profile (NHP) Questionnaire[116].

Reasons for non-completion of the assessment and/or questionnaire were recorded.

3.19 Staffing and Organisation

The project team consisted of the lead investigator (HR), the research fellow (CC), three consultant physicians with a specialist interest in stroke medicine, an engineer with expertise in the electrical stimulators, a project secretary, a database manager, and a project secretary. The project team met monthly to review progress and discuss issues arising. There was a research agenda at each meeting and minutes were kept. CC produced

progress reports and study updates for these meetings. A Gantt chart (Appendix 2.17) based upon project milestones was developed for project monitoring.

The research fellow (CC) was responsible for the day to day running of the project. As discussed in this chapter, CC identified eligible subjects, sought consent, undertook the initial assessments, and was responsible for training ward nursing staff and ensuring that the sNMES was given as per protocol. CC held regular update meetings for clinical staff. The nursing staff administered the sNMES and completed the diaries to indicate treatment sessions given or reasons for non-receipt of treatment. Two 'blinded' research nurses, trained by CC, collected the outcome data at 4 weeks and 3 months. A database was developed by the database manager/statistical advisor and data entry was undertaken by the project secretary. The study database generated appointment dates and facilitated project management. CC supervised the data entry and analysis.

3.20 Database and data quality checks

All information from the initial assessments, diaries, 4-week and 3-month assessments was entered on to the database which was specifically designed for the study. Data was checked for quality and completeness on a regular basis. The database manager and project secretary ensured that data collection was complete. Any data discrepancies were identified at project meetings and data subsequently cleaned and re-entered if necessary. Outcomes of intervention and control groups were not compared until the final 3-month assessment had been completed.

3.21 Data analysis

The study was analysed on an intention to treat basis using SPSS. Comparative analyses of most of the non-parametric data were made using the Mann-Whitney U Test. For the analysis of data with only a few categories, a chi square test was used. The significance level was p=0.05. There was one pre-planned subgroup analysis: participants with mild/moderate upper limb functional impairment (ARAT[6, 7] score > 0) were compared with those with severe functional impairment (ARAT[6, 7] score =0).

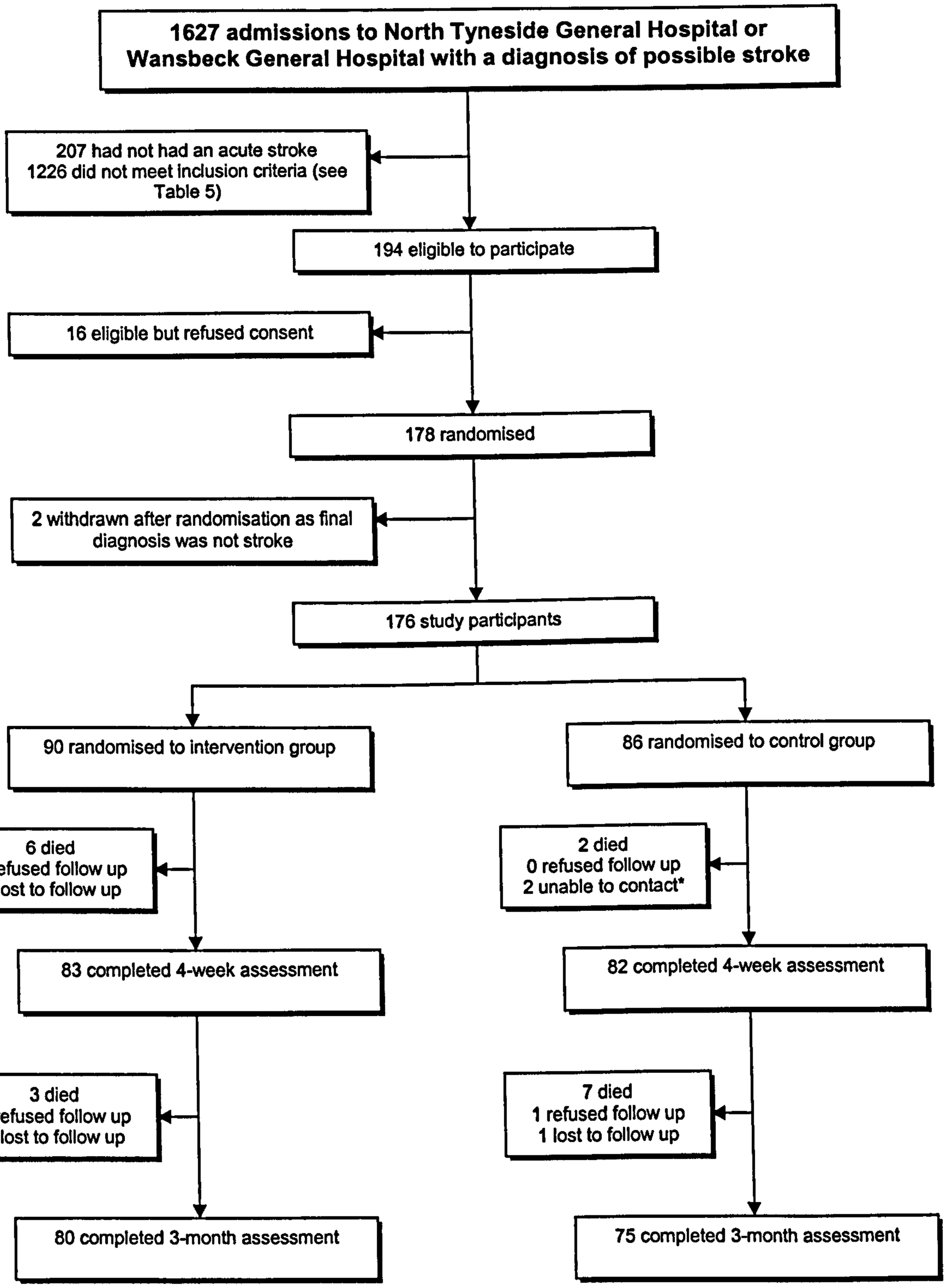
Chapter 4 Randomised Controlled Trial Results

4.1 Recruitment

Between 1st January 2002 and 29th February 2004, 1627 subjects were admitted to the stroke wards at NTGH and WGH with a diagnosis of possible stroke. A total of one hundred and seventy six subjects participated in the study. Figure 4 shows the study profile.

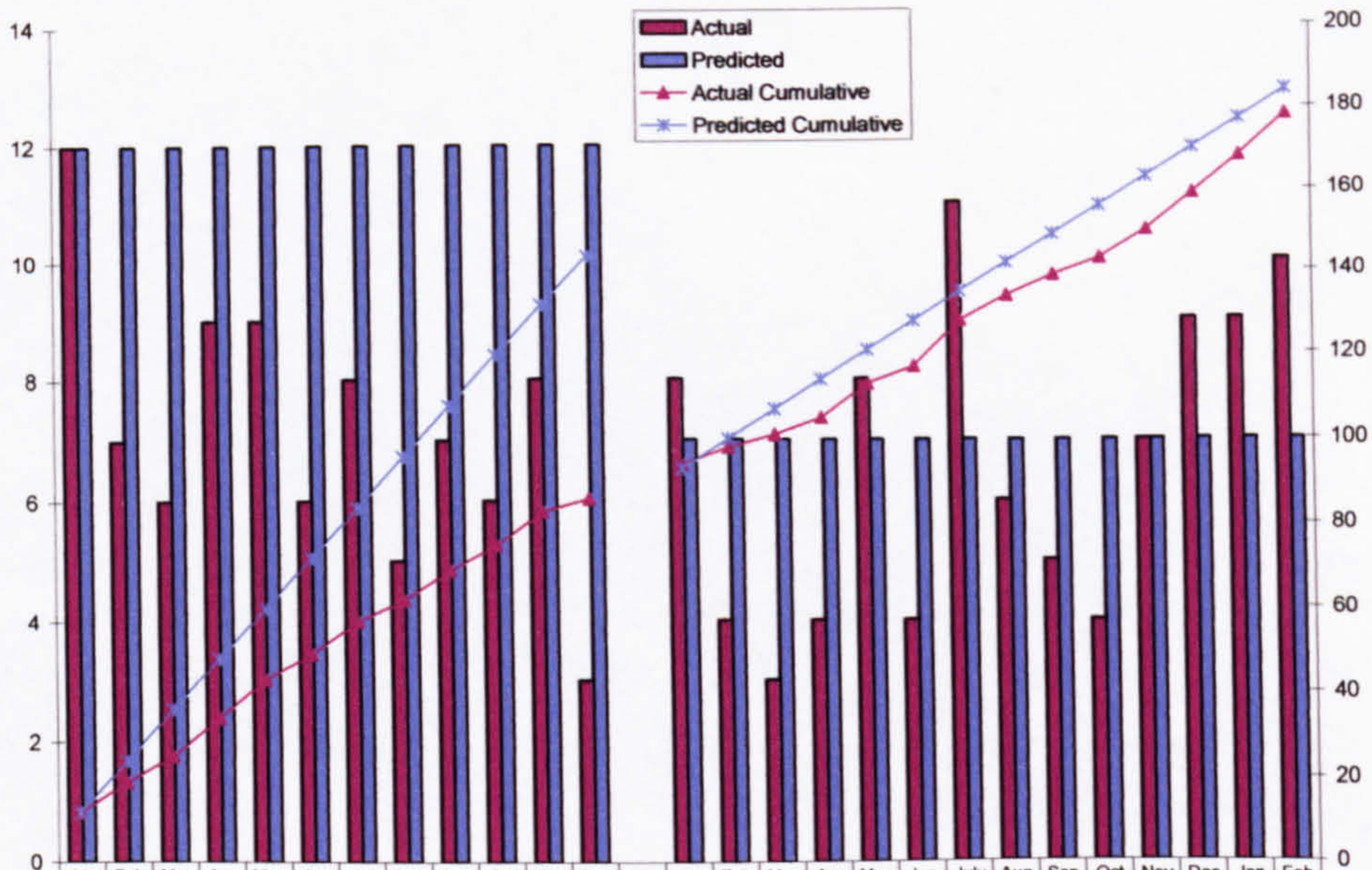
Based on stroke admission rates and data from previous studies, we initially anticipated that we would recruit 12 subjects per month over a 17-month period. However our initial recruitment rate was 7 per month. At the start of the study, subjects admitted to WGH who were resident in the catchment area for Blyth Community Hospital, Alnwick Infirmary and Berwick Infirmary were excluded for logistical reasons. Since the recruitment rate was lower than predicted, the study was expanded at the start of July 2002 to include those subjects resident in the catchment area for Blyth Community Hospital. At the end of 2002, the actual recruitment rate had remained low, so the predicted recruitment rate was adjusted to 7 per month and the recruitment period extended to a total of 26 months (Figure 5).

Figure 4: Study Profile



* 4-week assessment was not completed for 2 of the control subjects but 3-month assessment was completed for both

Figure 5: Actual and predicted numbers randomised by month



	Jan 2002	Feb 2002	Mar 2002	Apr 2002	May 2002	Jun 2002	Jul 2002	Aug 2002	Sep 2002	Oct 2002	Nov 2002	Dec 2002	Jan 2003	Feb 2003	Mar 2003	Apr 2003	May 2003	Jun 2003	July 2003	Aug 2003	Sep 2003	Oct 2003	Nov 2003	Dec 2003	Jan 2004	Feb 2004
Actual	12	7	6	9	9	6	8	5	7	6	8	3	8	4	3	4	8	4	11	6	5	4	7	9	9	10
Predicted	12	12	12	12	12	12	12	12	12	12	12	12	7	7	7	7	7	7	7	7	7	7	7	7	7	7
Actual Cumulative	12	19	25	34	43	49	57	62	69	75	83	86	94	98	101	105	113	117	128	134	139	143	150	159	168	178
Predicted Cumulative	12	24	36	48	60	72	84	96	108	120	132	144	93	100	107	114	121	128	135	142	149	156	163	170	177	184

4.2 Reasons for exclusion

One thousand two hundred and twenty six subjects with acute stroke were excluded as they did not meet the eligibility criteria. The commonest reasons for exclusion were no upper limb deficit (28%), living outside the area (19%), not within 10 days of stroke (12%), and receptive dysphasia (9%) (Table 5). Sixteen eligible subjects declined to take part in the study.

Table 5: Main reasons for exclusion (n=1226)

- 343 (28%) had no upper limb deficit
- 241 (19%) lived outside the area
- 154 (12%) were not within 10 days of stroke
- 106 (9%) had a significant receptive dysphasia
- 70 (6%) were medically unstable
- 58 (5%) scored >3 on the pre-stroke Oxford Handicap Scale
- 51 (4%) were discharged home prior to screening
- 49 (4%) had previous upper limb impairment
- 40 (3%) had a significant cognitive deficit
- 34 (3%) had another diagnosis likely to interfere with rehabilitation
- 31 (2%) scored <5 on the Glasgow Coma Scale
- 22 (2%) died prior to screening
- 10 (1%) had a permanent pacemaker/implantable defibrillator
- 10 (1%) other e.g. participation in another research trial
- 5 (<1%) had a diagnosis of recent shoulder fracture/dislocation (stroke-affected side)
- 2 (<1%) were taking regular analgesia for the upper limb (stroke-affected side)

4.3 Initial Assessment

4.3.1 Baseline characteristics and upper limb assessment

One hundred and seventy eight subjects were randomised but two were withdrawn immediately after randomisation as their final diagnosis was not stroke. Therefore, 176 subjects participated in the study, 90 randomised to the intervention group and 86 to the control group (Figure 4). The median time from stroke to randomisation was 5 days [IQR 4-7] for the intervention group and 4 days [IQR 3-7] for the control group.

Table 6: Demographics and pre-stroke characteristics (n=176)

		Intervention (n=90)	Control (n=86)
Sex – n (%)	Male	42 (46.7%)	47 (54.7%)
	Female	48 (53.3%)	39 (45.3%)
Median [IQR] age (years)	All	75.5 [64-81]	73.5 [65.8-79]
	Male	73.5 [62.3-82]	71 [63-76]
	Female	77 [64.3-80.8]	76 [69-82]
Oxford Handicap Scale[195] (pre-stroke) – n (%)			
0 – no symptoms		43 (48%)	36 (42%)
1 – few symptoms, not interfering with daily life		11 (12%)	15 (17%)
2 – symptoms changing life, can look after self		32 (36%)	27 (31%)
3 – symptoms changing life, need some help to look after self		4 (4%)	8 (9%)
Nottingham E-ADL[110] Index(pre-stroke)–median [IQR]			
	Mobility	5 [5-6]	5 [3.8-6]
	Kitchen	5 [5-5]	5 [4-5]
	Domestic	3 [2-4]	3 [2-4]
	Leisure	4 [2-4]	3 [2-4]
	Total	17 [15-18]	16 [12.8-18]
Previous stroke – n (%)		17 (19%)	15 (17%)
Previous stroke affecting same side – n (%)		7 (4%)	12 (14%)

The demographics and pre-stroke characteristics are shown in Table 6. There was a higher percentage of females in the intervention group but this difference was not statistically significant. Randomisation groups were well matched for age, pre-stroke handicap and Extended Activities of Daily Living (measured by the Oxford Handicap Scale[195] and Nottingham E-ADL[110] Index respectively). The scores in the mobility subsection of the Nottingham E-ADL Index were higher in the intervention group compared to controls, but this difference did not reach statistical significance.

Stroke type and impairment is shown in Table 7. One hundred and sixty four (93%) strokes were due to cerebral infarction. In terms of stroke subtype, the participants were well-matched between groups. More participants had left sided impairment in both randomisation groups because many right sided strokes were excluded due to the presence of receptive dysphasia. A greater number of participants in the intervention group had visuospatial

deficits at baseline compared with those in the control group although this difference did not reach statistical significance. There were no statistically significant differences between the groups in terms of stroke severity (National Institute of Health Stroke Scale[197], Barthel ADL Index[92]), visuospatial impairment (Star Cancellation Test[79]), cognition (Abbreviated Mental Test Score[159]) and aphasia (Sheffield Aphasia Screening Test[199]).

Table 7: Stroke type and impairment (n=176)

		Intervention (n=90)	Control (n=86)
Stroke type – n (%)	Infarct	86 (96%)	78 (91%)
	Haemorrhage	4 (4%)	8 (9%)
Stroke subtype[198] – n (%)			
Total anterior circulation stroke		29 (32%)	24 (28%)
Partial anterior circulation stroke		23 (26%)	23 (27%)
Lacunar stroke		36 (40%)	37 (43%)
Posterior circulation stroke		2 (2%)	2 (2%)
Unilateral weakness affecting face - n (%)		66 (73%)	62 (72%)
Unilateral weakness affecting arm/hand		89 (99%)	84 (98%)
Unilateral weakness affecting leg/foot		86 (96%)	80 (93%)
Sensory deficit affecting face		15 (17%)	14 (16%)
Sensory deficit affecting arm/hand		40 (44%)	41 (48%)
Sensory deficit affecting leg/foot		38 (42%)	38 (44%)
Dysphasia		12 (13%)	19 (22%)
Homonymous hemianopia		30 (33%)	28 (33%)
Visuospatial disorder		45 (50%)	30 (35%)
Brainstem/cerebellar signs		2 (2%)	3 (3%)
Other deficit		0 (0%)	1 (1%)
Side of upper limb impairment – n (%)	Right	31 (34%)	33 (38%)
	Left	59 (66%)	53 (62%)
National Institute of Health Stroke Scale[197]			
	Median [IQR]	8.5 [6-12]	9 [5-12.3]
Star Cancellation Test[79, 80] fail (Score <=51)–n (%)		38 (42%)	31 (36%)
Sheffield Aphasia Screening Test[199] – median [IQR]			
	Age <59 (n=28)	19 [19-19.8]	19 [18-19]
	Age 60-69 (n=32)	19 [18-20]	19 [17.5-20]
	Age 70+ (n=116)	18 [15-19]	17 [14-19]
Abbreviated Mental Test Score[159] – median [IQR]		9 [8-10]	9 [7.8-10]
Barthel ADL Index[92] 7 days after stroke – median [IQR]		8 [4-14.8]	10 [5.8-15.0]

In the initial upper limb assessment (Table 8), as discussed above, there were more participants with left sided upper limb impairment in both randomisation groups. Six participants (7%) in the control group reported pain pre-stroke compared with two (2%) in the intervention group but this difference was not statistically significant. The prevalence of upper limb pain following stroke at the initial assessment was similar between groups. The participants were well matched in terms of baseline upper limb impairment and disability (Motricity Index[9], Shoulder Shrug Test[71], Frenchay Arm Test[8], and Action Research Arm Test (ARAT)[6, 7]). Although many participants had reasonable upper limb muscle strength (arm Motricity Index[9] median scores of 57.5 in the intervention group, 60.5 in controls), most had no useful upper limb function (indicated by scores of 0 on the ARAT[6, 7] and

Frenchay Arm Test[8]). There was no difference in terms of the presence of cerebellar signs and sensory symptoms between randomisation groups.

Table 8: Initial upper limb assessment (affected side) (n=176)

		Intervention (n=90)	Control (n=86)
Handedness – n (%)	Right	82 (91%)	78 (91%)
	Left	7 (8%)	6 (7%)
	Ambidextrous	1 (1%)	1 (1%)
	Uncertain	0 (0%)	1 (1%)
Current stroke affecting dominant hand–n(%)	Yes	32 (36%)	32 (37%)
	No	58 (64%)	54 (63%)
Side of upper limb impairment – n (%)	Right	31 (34%)	33 (38%)
	Left	59 (66%)	53 (62%)
Upper limb pre-stroke pain – n (%)		2 (2%)	6 (7%)
Upper limb post-stroke pain – n (%)		21 (23%)	22 (26%)
Motricity Index[9] (Scale of 1-100)	median [IQR]		
	Arm	57.5 [12-77]	60.5 [14.3 -77]
	Leg	70 [43-84]	70 [43-84]
	Total	61.3 [36-82.4]	63.3 [36.4-78.1]
Shoulder Shrug Test[7] – n (%)	median[IQR]	1 [1-2]	1 [1-1]
0 = no movement		16 (18%)	14 (16%)
1 = reduced movement		49 (54%)	52 (61%)
2 = normal movement		25 (28%)	20 (23%)
Frenchay Arm Test[8]	median [IQR]	0.5 [0-4]	0 [0-4]
Action Research Arm Test (ARAT)[6, 7] (Scale 1-57)	median[IQR]	n=89	n=83
Total		0 [0-45.5]	3 [0-47]
Grasp		0 [0-15]	0 [0-16]
Grip		0 [0-10.5]	0 [0-10]
Pinch		0 [0-12]	0 [0-12]
Gross		0 [0-9]	3 [0-9]
Number (%) of those with baseline ARAT = 0		45 (51%)	39 (47%)
Number (%) of those with baseline ARAT > 0		44 (49%)	44 (53%)
National Institute for Health Stroke Scale[19?] – best motor arm – n (%)		n=90	n=86
0 – no drift		6 (7%)	8 (9%)
1 – drift after brief hold		36 (40%)	37 (43%)
2 – cannot resist gravity		15 (17%)	12 (14%)
3 – no effort against gravity		33 (37%)	29 (34%)
Cerebellar signs – n (%)		2 (2%)	3 (3%)
Sensory symptoms – n (%)		41 (46%)	41 (48%)

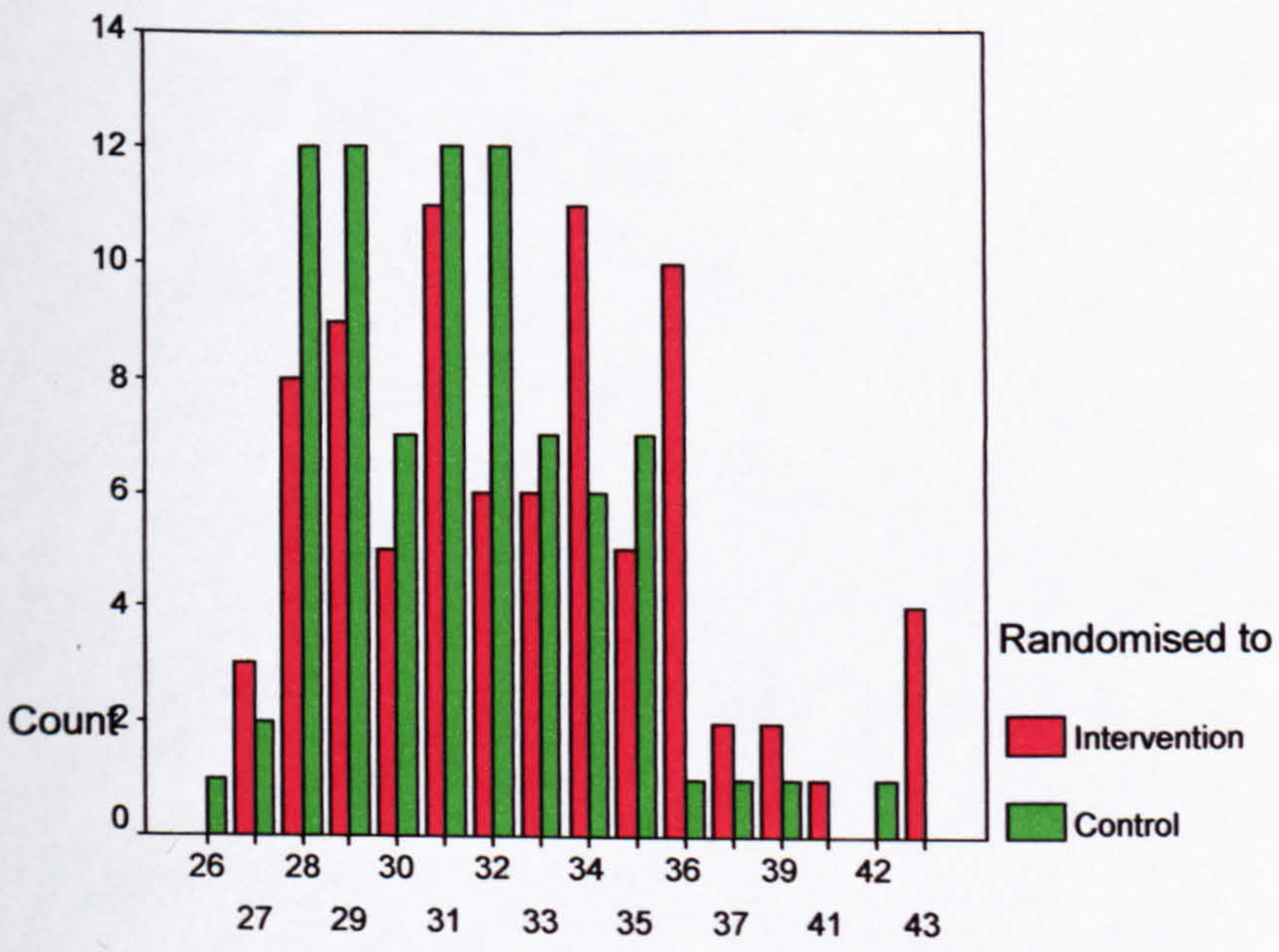
* ARAT performed in 154 participants (76 intervention, 76 controls); 20 subjects (13 intervention, 7 controls) were unable to sit and therefore scored 0. The ARAT was not performed in 4 participants (1 intervention-felt unwell/dizzy. 3 controls-2 subjects unavailable; ARAT table unavailable for one subject).

4.4 Follow up assessments

4.4.1 Four-week outcomes

One hundred and sixty five participants completed the four-week assessments: 83 in the intervention group and 82 in the control group. Eight participants died prior to the 4-week assessment (Table 9), and one (in the intervention group) refused follow up although was alive and in private residence at the time that this assessment was due. We were unable to contact two participants within the timescale of the 4-week assessment. Both of these participants however completed the assessments at 3 months.

Figure 6: Days from randomisation to 4-week review



According to the study protocol, the 4-week assessment was to be done between days 29 and 36 after randomisation. Participants in the intervention group were seen a median of 32 days (range 27 to 43), and those in the control group a median of 31 days (range 26 to 42) after randomisation (Figure 6).

There were no statistically significant differences between the groups in terms of current residence. More participants in the control group had been readmitted to hospital prior to the 4-week review than those in the intervention group but this difference was not statistically

significant. The prevalence of new upper limb problems (stroke-affected side) was similar between groups (Table 9).

Table 9: 4-week mortality, placement and dependence

	Intervention (n=90)	Control (n=86)	P value
Dead – n (%)	6 (7%)	2 (2%)	0.279
Institutionalised (nursing home/ residential home/hospital)	n=84 42 (50%)	n=84 35 (42%)	0.353
Oxford Handicap Scale (OHS)[195] median [IQR]	n=83 3 [2-5]	n=82 3 [2-5]	0.721
Barthel ADL Index[92] median [IQR]	n=83 14 [9-18]	n=82 15 [6-19]	0.952
Dead or dependent (OHS[195] 3-5)	n=89 62 (70%)	n=84 62 (74%)	0.663
Dead or dependent (Barthel[92] <19/20)[201]	n=89 69 (78%)	n=84 60 (71%)	0.456
Dead or institutionalised	n=90 48 (53%)	n=86 37 (43%)	0.223
Readmission to hospital - n (%)	n=83 2 (2%)	n-82 5 (6%)	0.277
Recurrent stroke*	1 (1%)	1 (1%)	1.000
New upper limb problems – n (%)** (affected side)	3 (4%)	2 (2%)	1.000

* Did not report new upper limb problems resulting from their recurrent stroke.
** New upper limb problems all secondary to new trauma

There were no statistically significant differences between the groups in any of the upper limb outcome measures at 4 weeks i.e. upper limb impairment and disability (ARAT score[6], FAT score[8], Motricity Index[9], Shoulder Shrug Test[71], and Star Cancellation Test[79]), and upper arm girth[133] (Table 10). The pain assessment was similar between groups in terms of presence of pain in the affected upper limb, severity of pain[127, 128], pain-free range of humeral lateral rotation[130, 131], and the number of participants receiving analgesia or other interventions for upper limb pain since their stroke (Table 11).

Table 10: 4-week upper limb outcome measures (affected side)

	Intervention (n=83)	Control (n=82)	P value
ARAT[6, 7]*	n=81	n=82	
median [IQR]			
Total	45.0 [0-57]	45.5 [0-57]	0.888
Grasp	15 [0-18]	12 [0-18]	0.853
Grip	12 [0-12]	12 [0-12]	0.523
Pinch	12 [0-18]	11.5 [0-18]	0.818
Gross	9 [0-9]	9 [0-9]	0.885
FAT[8]	n=83	n=82	
median [IQR]	4 [0-5]	4 [0-5]	0.923
Motricity[9] Index	n=83	n=81	
median [IQR]			
Arm	77 [40-100]	81 [53-100]	0.574
Leg	76 [62-100]	84 [58.5-100]	0.940
Total	80 [52.5-93]	77 [62.5-96]	0.850
Shoulder Shrug Test[71]	n=83	n=81	
median [IQR]	2 [1-2]	2 [1-2]	0.183
n (%)			
0 = no movement	16 (19%)	11 (14%)	0.409
1 = reduced movement	25 (30%)	21 (26%)	
2 = normal movement	42 (51%)	49 (61%)	
Upper arm girth[133] in cm	n=78	n=79	
median [IQR]	31 [28-34]	32 [30-34]	0.353
Star Cancellation Test[79, 80]	n=83	n=82	
no. (%) failed	27 (33%)	28 (34%)	0.870

* ARAT performed in 143 participants (73 intervention, 70 controls); 20 participants (8 intervention, 12 controls) were unable to sit and therefore scored 0. The ARAT was not performed in 2 participants (intervention group) – 1 barrier nursed, 1 ARAT table unavailable.

Table 11: 4-week upper limb pain (affected side)

	Intervention (n=83)	Control (n=82)	P value
Upper limb pain[127, 128] – n (%)	22 (27%)	26 (32%)	0.462
If pain, median [IQR]			
5 point severity scale	3 [2-3.3]	3 [2-4]	0.227
0-10 numerical rating scale	5 [3-7.3]	5 [3.8-8]	0.770
Humeral lateral rotation - range pain free movement[130, 131] median [IQR]			
Passive*	n=80	n=79	
	90 [77-100]	90 [72-102]	0.901
Active**	n=81	n=77	
	72.0 [20-95.5]	70 [42.5-95]	0.614
Taking regular painkillers for upper limb pain – n (%)	n=83	n=82	
	18 (22%)	18 (22%)	1.000
Other interventions for upper limb pain since stroke – n (%)	n=83	n=82	
None	62 (75%)	63 (77%)	0.856
Oral analgesia	21 (25%)	17 (21%)	0.580
Steroid injection	0 (0%)	0 (0%)	-
TENS	2 (2%)	0 (0%)	0.497
Botulinum toxin	0 (0%)	0 (0%)	-
Other (amitryptiline)	0 (0%)	1 (1%)	0.497

* One participant (intervention group) not assessed as barrier nursed. Missing data for 5 participants (2 intervention and 3 controls).

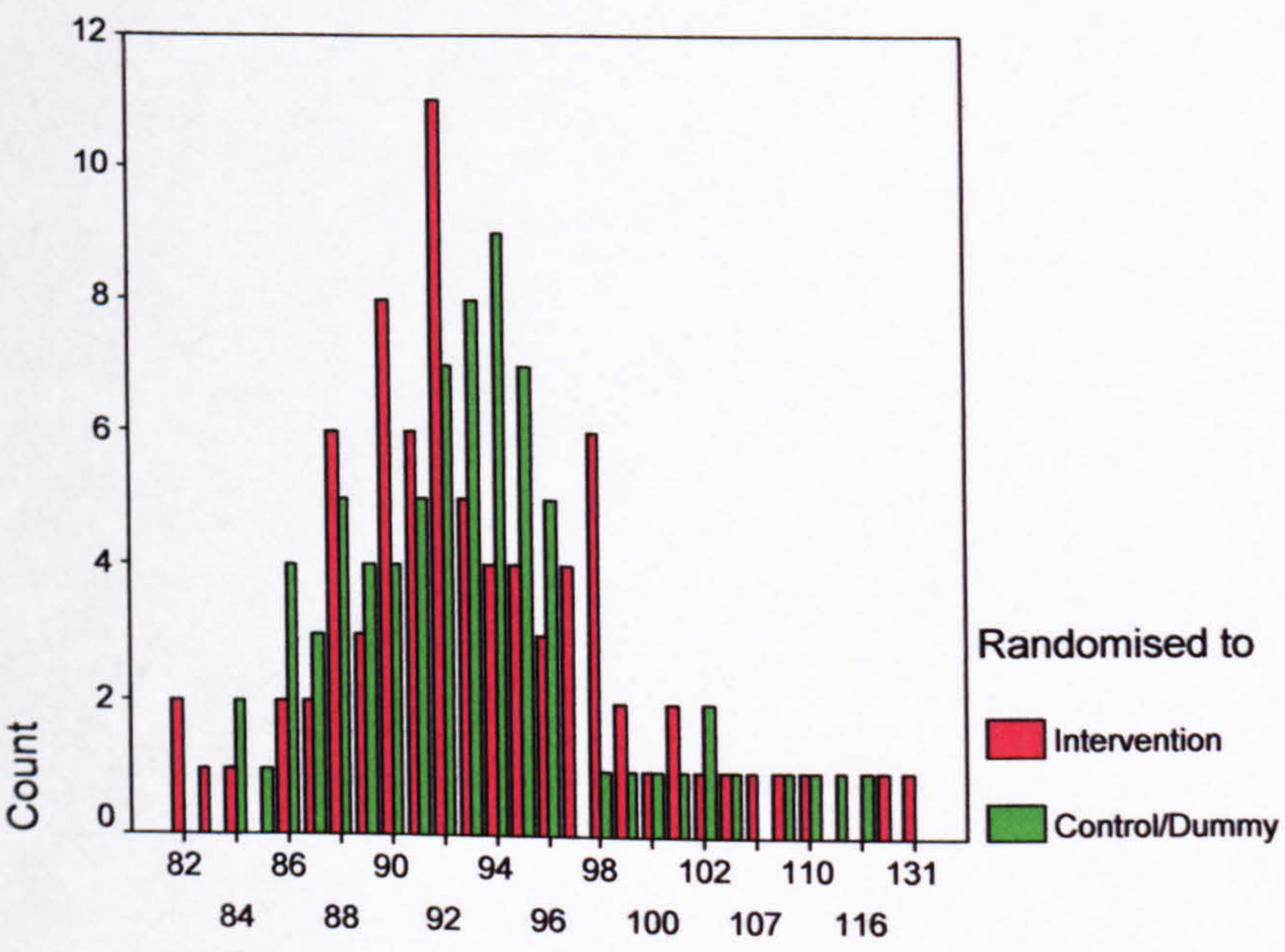
** Two participants (control group) unable to understand and one (intervention group) barrier nursed therefore not assessed. Missing data for 4 participants (1 intervention and 3 controls).

4.4.2 Three-month outcomes

One hundred and fifty five participants completed the 3-month assessment, 80 in the intervention group and 75 in the control group. Ten participants died between the 4-week and 3-month assessment (Figure 4). Eighteen participants (9 intervention and 9 controls) died during the 3-month study period (Table 12). One participant in the control group, in private residence at the time that the 3-month assessment was due, refused follow up at 3 months. Another participant in the control group was lost to follow up. They were alive and in private residence at the time that the 3-month assessment was due but we were unable to contact them.

According the study protocol, the 3-month assessment was to be done between days 83 and 97 post stroke. Participants in the intervention group were seen a median of 92 days (range 82 to 131), and those in the control group a median of 93 days (range 84 to 116) after randomisation (Figure 7).

Figure 7: Days from stroke to 3 month review



The majority of participants were in private residences at the time of the 3-month assessment, and there were no statistically significant differences between the groups in terms of current residence. The length of initial hospital stay was longer in the intervention group than the control group but this difference did not reach statistical significance. The

readmission rates since the 4-week assessment were similar between groups. The prevalence of new upper limb problems (stroke-affected side) was also similar between groups. There was no significant difference between groups in the number of participants still receiving physiotherapy at 3 months (Table 12).

Table 12: 3-month mortality, placement, dependence, and physiotherapy

	Intervention (n=90)	Control (n=86)	P value
Dead – n (%)	9 (10%)	9(10%)	0.883
Institutionalised (nursing home/residential home/hospital)	n=81 21 (26%)	n=77 17 (22%)	0.704
Oxford Handicap Scale (OHS)[195] n (%) median [IQR]	n=80 3 [2-4]	n=75 3 [2-4]	0.997
Barthel ADL index[92] median [IQR]	n=80 17.5 [11.3-20]	n=75 17 [14-20]	0.692
Dead or dependent (OHS[195] 3-5)	n=89 62 (70%)	n=84 59 (70%)	0.934
Dead or dependent (Barthel[92] <19/20)[201]	n=89 60 (67%)	n=84 55 (65%)	0.913
Dead or institutionalised	n=90 30 (33%)	n=86 26 (30%)	0.780
Length of initial hospital stay (days) median [IQR]	n=90 35.5 [17-58.6]	n=86 24.5 [12-63.3]	0.131
Readmission to hospital since 4 week assessment - n (%)	n=80 5 (6%)	n=75 5 (7%)	1.000
Readmission to hospital since stroke n (%)	n=80 7 (9%)	n=75 8 (11%)	0.895
Recurrent stroke	n=80 0 (0%)	n=75 1 (1%)	0.484
New upper limb problems (since 4 week assessment)* – n (%) (affected side)	n=80 2 (3%)	n=75 3 (4%)	0.674
Still receiving physiotherapy at 3 months n (%)	n=86 33 (43.4%)	n=85 25 (35.2%)	0.205

* In the intervention group, one was due to a frozen shoulder and the other to a swollen hand of unknown aetiology. In the control group, one was due to trauma, one to arthritis, and one to recurrent stroke.

The primary outcome measure was arm function as measured by the ARAT[6, 7] at 3 months after stroke (Table 13). Those in the control group achieved higher total scores than those in the intervention group (medians of 55.5 and 50.0 respectively) but this did not reach statistical significance. However, significant differences were seen in the grasp and gross subsections of the ARAT[6, 7], the controls achieving higher scores than the intervention group. The median [IQR] grasp score was 18 [12-18] in the control group and 12 [0-18] in the intervention group, and the median [IQR] gross score was 9 [9-9] in the control group and 9 [0-9] in the intervention group (p values of 0.014 and 0.015 respectively) (Table 13). Clinically, a difference of 3 on the ARAT[6, 7] reflects not being able to do a subtest and then to fully complete it.

Table 13: 3-month upper limb outcome measures (affected side)

	Intervention	Control	P value
ARAT[6, 7]*	n=79	n=74	
median [IQR]			
Total	50.0 [0-57]	55.5 [38.3-57]	0.068
Grasp	12 [0-18]	18 [12-18]	**0.014**
Grip	12 [0-12]	12 [8.8-12]	0.071
Pinch	15 [0-18]	18 [8.5-18]	0.155
Gross	9 [0-9]	9 [9-9]	**0.015**
FAT[8]	n=80	n=75	
median [IQR]	4 [0.3-5]	5 [3.0-5]	**0.014**
Motricity[9] Index	n=79	n=74	
median [IQR]			
Arm	84 [56-100]	93 [77-100]	**0.025**
Leg	92 [70-100]	86 [76-100]	0.948
Total	88 [66-100]	89 [76.5-100]	0.248
Shoulder Shrug Test[71]	n=79	n=74	
median [IQR]	2 [1-2]	2 [1-2]	0.108
n (%)			
0 (no movement)	9 (11%)	5 (7%)	0.273
1 (reduced movement)	23 (29%)	16 (22%)	
2 (normal)	47 (60%)	53 (72%)	
Upper arm girth[133] in cm	n=79	n=75	
median [IQR]	32 [28-35]	32 [30-35]	0.105
Star Cancellation Test[79, 80]	n=80	n=75	
number (%) of subjects failed	25 (31%)	18 (24%)	0.371

* ARAT performed in 153 participants (74 intervention, 70 controls); 9 participants (5 intervention, 4 controls) unable to sit = score 0; not performed in 2 participants (1 intervention, 1 control) as the ARAT Table was unavailable.

For the other measures of upper limb impairment and disability, the control group achieved higher scores on the FAT[8] and the Arm subsection of the Motricity Index[9] and these differences were statistically significant (Table 13). The median [IQR] FAT score was 5 [3.0-5] in the control group and 4 [0.3-5] in the intervention group, and the median [IQR] Arm Motricity Index score was 93 [77-100] in the control group and 84 [56-100] in the intervention group (p values of 0.014 and 0.025 respectively). Clinically, an improvement of 1 on the FAT[8] indicates being able to complete one of the 5 subtests that previously could not be done.

There were no statistically significant differences between the groups for the remaining upper limb outcome measures i.e. Shoulder Shrug Test[71], upper arm girth[133] and Star Cancellation Test[79] (Table 13). When assessing visuospatial impairment using the Star Cancellation Test[79], a greater percentage of participants failed this test in the intervention group compared to the controls but this was not statistically significant.

There were no statistically significant differences between groups in the upper limb pain assessment at 3 months (Table 14).

Table 14: 3-month upper limb pain (affected side)

	Intervention (n=80)	Control (n=75)	P value
Upper limb pain[127, 128] n (%)	37 (46%)	34 (45%)	0.963
If pain, median [IQR]			
5 point severity scale	3 [1-3]	3 [2-3]	0.429
0-10 numerical rating scale	6 [3.5-8]	7 [5-8]	0.651
Taking regular painkillers for UL pain–n (%)	25 (31%)	19 (25%)	0.477
Humeral lateral rotation - range of pain free movement[130, 131]			
median [IQR]			
Passive	90 [70-110]	89 [70-100]	0.924
Active	80 [40-95]	80 [50-96]	0.650
Other interventions for upper limb pain since stroke – n (%)			
None	58 (73%)	55 (73%)	1.000
Oral analgesia	22 (28%)	19 (25%)	0.856
Steroid injection	0 (0%)	0 (0%)	-
TENS	0 (0%)	0 (0%)	-
Botulinum toxin	0 (0%)	0 (0%)	-
Other	1 (1%)	1 (1%)	1.000

Assessment of disability using the Nottingham EADL Index[110], and global health status using the Nottingham Health Profile[116] showed no statistically significant differences between the groups at 3 months (Table 15). Although the median energy level and pain scores were higher in the control group than the intervention group, the inter-quartile ranges and distributions were similar between groups and the p values are therefore not statistically significant.

Table 15: 3-month disability and global health status

	Intervention	Control	P value
Nottingham-EADL[110] Index	n=80	n=74	
median [IQR]			
Mobility	1 [0-5]	2 [0-5]	0.209
Kitchen	3 [1-5]	3.5 [0-5]	0.807
Domestic	1 [0-2]	1 [0-3]	0.566
Leisure	2 [1-3]	2 [1-3]	0.551
Total	8 [2-15]	8.5 [2-15]	0.515
Nottingham Health Profile[116] median [IQR]	n=76	n=71	
Energy level	39.2 [24-100]	60.8 [24-100]	0.998
Pain	10.2 [0-37.4]	18.7 [0-38.2]	0.673
Emotional reactions	18.3 [0-56.0]	17.6 [7.1-40.6]	0.756
Sleep	34.6 [0-77.6]	12.6 [0-50.4]	0.063
Social isolation	0.0 [0-41.2]	0 [0-34.5]	0.793
Physical abilities	44.3 [13.5-57.2]	43.9 [11.6-57.3]	0.988
Mean of subscales	31.2 [10.4-52.1]	28.1 [15.7-48.2]	0.577

4.4.2.1 Participants' views about sNMES

In rehabilitation studies, it can be difficult to blind participants and assessors to treatment group allocation. Many previous studies did not use a sham treatment for control participants as we have in this study. In addition, many have not reported whether outcome assessors were blinded to treatment group allocation.

We were initially concerned that control participants in this study would be aware that they were receiving 'sham' treatment but this has not been the case. In the intervention group, when participants were asked (at 3 months) which stimulator they had been given, 71% thought that they had been given the 'real' stimulator, 1% the 'dummy' stimulator and 28% were uncertain. In the placebo group, 20% thought that they had been given the 'real' stimulator, 24% the 'dummy' stimulator and 55% were uncertain (Table 16). That is, the percentage of those participants correctly identifying the type of stimulator was 71% in the intervention group and 24% in the control group. Overall, 49% of participants correctly identified their stimulator. Many more participants in the control group than the intervention group were uncertain about which type of stimulator they had received. This may have been because most of the controls did not experience any symptoms from their stimulator.

Table 16: Experience and views of participants about sNMES

Participants' views about sNMES	Intervention (n=80)	Control (n=74)	P value
Correct about type of stimulator received – n (%)	57 (71%)	18 (24%)	<0.001
Incorrect about type of stimulator received – n (%)	1 (1%)	15 (20%)	<0.001
Unsure about type of stimulator received – n (%)	22 (28%)	41 (55%)	<0.001
Symptoms from the stimulator e.g. tingling – n (%)	68 (85%)	15 (20%)	<0.001
Pain from the stimulator – n (%)	14 (18%)	1 (1%)	0.002

In the intervention group, 85% of participants experienced symptoms from the stimulator, and 18% attributed upper limb pain to the stimulator. In contrast, 23% of participants in the control group reported experiencing symptoms from the stimulator and 1% experienced pain (Table 16).

Participants were also asked to give general comments regarding their experience of the sNMES. In 67% of cases, comments were positive or neutral. In 22%, the comments were negative, and 11% of participants made no comment. In the intervention group, 59% were positive/neutral, 30% negative, and 11% made no comment. This was compared with

percentages of 75%, 15% and 11% respectively in the control group. Positive comments included "felt like a massage when the machine was on"; "felt more relaxed when the machine was on"; "lovely – relaxing". Neutral comments included "no bother"; "can't remember having it on"; "felt nothing at all – no problem". Negative comments included "uncomfortable at times"; did not like feeling tied down to machine"; "did not like it – got in the way of her clothes".

Previous studies of upper limb sNMES which used a sham stimulator did not ask participants to comment on treatment group allocation or to give views regarding the stimulator.

4.5 Summary of RCT results

- There was no statistically significant difference in arm function between groups for the primary outcome measure (total ARAT[6, 7] score at 3 months after stroke).
- There were, however, significant differences in outcomes in favour of the control group when using other measures to assess arm function at 3 months (the grasp and gross subsections of the ARAT[6, 7], and the FAT[8]).
- There was also a significant difference in favour of the control group when measuring upper limb impairment at 3 months using the Arm Motricity Index[9].
- These results were surprising and the reasons unclear.
- There were no statistically significant differences between the randomisation groups at 4 weeks.
- There were no statistically significant differences between the randomisation groups at baseline, in particular stroke subtype, cognition, pain and visuospatial deficit.
- We undertook a post-hoc exploratory analysis to try to explain the differences seen between randomisation groups at 3 months.

Chapter 5 Subgroup and Secondary Analyses

The main randomised controlled trial results (Chapter 4) found no statistically significant difference in arm function between the randomisation groups for the primary outcome measure. However, significant differences were seen at 3 months in favour of the control group when using other measures to assess arm function. No statistically significant differences were seen between groups at 4 weeks.

There were no obvious confounding factors to explain these results at 3 months in favour of the control group. The randomisation groups were similar at baseline, in particular, stroke subtype, pain and visuospatial deficit. More participants in the control group (n=9) dropped out between 4 weeks and 3 months compared with participants in the intervention group (n=3) (Figure 4). We analysed these dropouts in terms of their demographics and 4-week outcome measures to see if there were any differences between groups which may have confounded the results. Four-week outcome measurements for these participants are shown in Table 17. If the dropouts in the control group were more impaired at 4 weeks than those in the intervention group, this could have explained, at least in part, why the control group achieved better scores at 3 months in the measures of function and impairment. However, this was not the case and the controls were in fact less impaired at 4 weeks than those in the intervention group (Table 17).

Table 17: 4-week outcomes for participants who dropped out of the study between 4 weeks and 3 months

		Intervention (n=3)	Control (n=9)
Sex – n (%)	Male Female	1 (33%) 2 (67%)	3 (33%) 6 (67%)
Median [IQR] age (years)	All Male Female	77 [76-*] 76 [*] 78.5 [77-*]	72 [69.5-81.5] 75 [72-*] 71 [68-80.8]
Institutionalised (nursing home/ residential home/hospital) – n (%)		3 (100%)	8 (89%)
Oxford Handicap Scale (OHS)[195]	Score 3 Score 5	0(0%) 3 (100%)	3 (33%) 6 (67%)
Barthel ADL Index[92]	median [IQR]	2 [0-*]	2 [0-17.5]
Recurrent stroke		0 (0%)	0 (0%)
ARAT[6, 7]	median [IQR]		
Total		0.0 [0-0]	0 [0-22.5]
Grasp		0.0 [0-0]	0 [0-6]
Grip		0.0 [0-0]	0 [0-6]
Pinch		0.0 [0-0]	0 [0-6]
Gross		0.0 [0-0]	0 [0-4.5]
FAT[8]	median [IQR]	0 [0-0]	0 [0-2.5]
Motricity Index[9]		n=3	n=8
	median [IQR]		
	Arm	1 [1-*]	54.5 [12-84]
	Leg	1 [1-*]	71.5 [44.3-90]
	Total	1 [1-*]	67.8 [29.5-83.9]
Shoulder Shrug Test[71]		n=3	n=8
	median [IQR]	0 [0-0]	1 [0.3-2]
Star Cancellation Test[79, 80]			
	no. (%) failed	3 (100%)	9 (100%)
Upper limb pain[127, 128, 130, 131] – n (%)		1 (33%)	3 (33%)
If pain, median [IQR]			
5 point severity scale		2 [*-*]	3 [2-*]
0-10 numerical rating scale		9 [*-*]	5 [1-*]

* Unable to calculate due to small numbers

There was one pre-planned subgroup analysis to look at the outcomes of participants with mild/moderate upper limb function (ARAT>0) and those with severe functional impairment (ARAT=0) at the initial assessment. There is evidence that the severity of initial upper limb motor impairment is a predictor of upper limb recovery[3, 65]. There is also evidence that ES is more beneficial in stroke patients with a milder degree of upper limb impairment[155].

5.1 Outcomes according to initial arm function

5.1.1 Outcomes at 4 weeks, according to initial arm function

There were no statistically significant differences between the groups for mortality, placement or dependency (measured by the OHS[195] and Barthel ADL Index[92]) at 4 weeks when the outcomes were analysed according to initial arm function (ARAT=0 vs. ARAT>0) (Table 18).

Table 18: 4-week mortality, placement and dependency, according to initial arm function

	Intervention	Control	P value	Intervention	Control	P value
	ARAT=0 n=45	ARAT=0 n=39		ARAT>0 n=44	ARAT>0 n=44	
Dead n (%)	6 (13%)	2 (5%)	0.275	-	-	
Institutionalised (NH/RH/hospital) n (%)	n=39 31 (79%)	n=37 26 (70%)	0.508	n=44 10 (23%)	n=44 9 (20%)	1.000
Dependent (Barthel<19/20) n(%)	n=39 37 (95%)	n=37 34 (92%)	0.671	n=43 25 (58%)	n=42 21 (50%)	0.592
OHS[195] median [IQR]	n=39 5 [3-5]	n=37 5 [3-5]	0.551	n=43 2 [2-4]	n=42 3 [2-3]	0.469
Barthel ADL Index[92] median [IQR]	n=39 9 [4-13]	n=37 6 [2.5-15.5]	0.617	n=43 18 [15-20]	n=42 18 [14-18]	0.477

Table 19: 4-week affected upper limb outcomes, according to initial arm function

	Intervention	Control	P value	Intervention	Control	P value
	ARAT=0 n=39	ARAT=0 n=37		ARAT>0 n=43	ARAT>0 n=42	
ARAT[6, 7] median [IQR]	n=37 0 [0-20.5]	n=37 0 [0-43]	0.917	n=43 57 [48-57]	n=42 53.5 [44.8-57]	0.200
Grasp	0 [0-7]	0 [0-12]	0.702	18 [18-18]	18 [12-18]	0.054
Grip	0 [0-4.5]	0 [0-12]	0.555	12 [12-12]	12 [12-12]	0.937
Pinch	0 [0-1.5]	0 [0-8.5]	0.520	18 [12-18]	18 [10.3-18]	0.547
Gross	0 [0-9]	0 [0-9]	0.844	9 [9-9]	9 [9-9]	0.417
FAT[8] median [IQR]	n=39 0 [0-2]	n=37 0 [0-2.5]	0.602	n=43 5 [4-5]	n=42 5 [4-5]	0.197
Motricity[9] Index median [IQR]	n=39	n=36		n=43	n=42	
Arm	40 [1-77]	53 [29.3-77]	0.348	93 [84-100]	93 [77-100]	0.807
Leg	76 [34-84]	62 [34.3-84]	0996	92 [76-100]	92 [70-100]	0.664
Total	57 [22-78]	64.5 [30-76]	0.702	88 [81.5-100]	92 [76.9-100]	0.768
Star cancellation test[79, 80] fail n (%)	n=39 19 (49%)	n=37 23 (62%)	0.258	n=43 7 (16%)	n=42 5 (12%)	0.757
Shoulder Shrug Test[71] median [IQR]	n=39 1 [0-1]	n=36 1 [0-2]	0.401	n=43 2[1-2]	n=42 2 [2-2]	0.317
Upper arm girth[133] in cm median [IQR]	n=36 29 [26.3-32]	n=35 31 [30-34]	0.091	n=42 32 [29-35.6]	n=41 33 [29.5-34]	0.766

No statistically significant differences between the groups were seen in any of the upper limb outcome measures when the 4-week outcomes were analysed according to initial arm function i.e. upper limb impairment and disability (ARAT[6, 7], FAT[8], Motricity Index[9], Star Cancellation Test[79, 80], and Shoulder Shrug Test[71]), and upper arm girth[133] (Table 19).

There were also no significant differences between groups for the affected upper limb pain assessment[127, 128, 130, 131] at 4 weeks, according to initial arm function (Table 20).

Table 20: 4-week upper limb pain (affected side)[127, 128, 130, 131], according to initial arm function

	Intervention	Control	P value	Intervention	Control	P value
	ARAT=0	ARAT=0		ARAT>0	ARAT>0	
Pain	n=39	n=37		n=43	n=42	
Affected side – n (%)	17 (44%)	16 (43%)	0.841	5 (12%)	10 (24%)	0.235
If Pain	n=17	n=16		n=5	n=10	
Severity scale – median [IQR]	3 [1.5-3.5]	3[2-4]	0.402	3 [2.5-3.5]	3.5 [2-4]	0.679
Numerical rating scale – median [IQR]	5 [3.5-8]	5 [2.5-8]	0.901	5 [2-6.5]	6 [4.5-7.3]	0.371
Humeral lateral rotation – median [IQR]						
Passive	n=37	n=34		n=43	n=42	
	82 [63.5-94.5]	84.5 [60-97]	0.403	95 [82-110]	90 [79-110]	0.334
Active	n=37	n=32		n=43	n=42	
	40 [0-72.5]	60 [0-84.3]	0.340	85 [70-100]	80 [63.8-100]	0.408

5.1.2 Outcomes at 3 months according to initial arm function

There were no statistically significant differences between the groups for mortality, placement and dependency (measured by the OHS[195] and Barthel ADL Index[92]) at 3 months when participants were analysed according to initial arm function (Table 21).

Table 21: 3-month mortality, placement and dependency, according to initial arm function

	Intervention	Control	P value	Intervention	Control	P value
	ARAT=0 n=45	ARAT=0 n=39		ARAT>0 n=44	ARAT>0 n=44	
Dead n (%)	8 (18%)	7 (18%)	0.791	0 (0%)	2 (5%)	0.494
Institutionalised (NH/RH/hospital) n (%)	n=37 19 (51%)	n=32 13 (41%)	0.516	n=44 2 (5%)	n=42 4 (9%)	0.428
Dependent (Barthel <19/20) n (%)	n=37 31 (84%)	n=30 23 (77%)	0.452	n=43 20 (47%)	n=42 21 (50%)	0.829
OHS[195] median [IQR]	n=37 4 [3-5]	n=30 4 [3-5]	0.974	n=43 2 [1-3]	n=42 3 [2-3]	0.358
Barthel ADL index[92] median [IQR]	n=37 14 [7-18]	n=30 14.5 [5-18.5]	0.815	n=43 19 [17-20]	n=42 18.5 [16-20]	0.465

In those participants scoring 0 on the ARAT[6, 7] at baseline, differences were seen between the groups in favour of the control group for the assessment of arm function. The median total ARAT[6, 7] score at 3 months was greater in the control group than the intervention group but this difference did not reach statistical significance. There were, however, statistically significant differences in favour of the control group in the grasp and gross subsections of the ARAT[6, 7] (Table 22).

For the other measures of upper limb impairment and disability, there were again differences in favour of the control group when analysing participants who scored 0 on the ARAT[6, 7] at the initial assessment. The control group achieved higher scores on the FAT[8] and the Arm Motricity Index[9], and the difference in the Arm Motricity Index scores reached statistical significance.

In the ARAT=0 group, no other statistically significant differences were seen for the other upper limb outcome measures i.e. the Star Cancellation Test[79, 80], Shoulder Shrug Test[71], and upper arm girth[133] (Table 22).

Table 22: 3-month upper limb outcomes (affected side), according to initial ARAT[6, 7] score

	Intervention	Control	P value	Intervention	Control	P value
	ARAT=0	ARAT=0		ARAT>0	ARAT>0	
ARAT[6, 7] median [IQR]	n=37	n=30		n=42	n=41	
Total	0 [0-33.5]	34.5 [0-54]	0.057	57 [51-57]	57 [52.5-57]	0.690
Grasp	0 [0-6]	11 [0-18]	**0.049**	18 [17.3-18]	18 [18-18]	0.201
Grip	0 [0-12]	9.5 [0-12]	0.124	12 [12-12]	12 [12-12]	0.673
Pinch	0 [0-6]	3 [0-17.3]	0.179	18 [16.5-18]	18 [16-18]	0.963
Gross	0 [0-9]	9 [0-9]	**0.034**	9 [9-9]	9 [9-9]	0.444
FAT[8] median [IQR]	n=37 0.0 [0-3.5]	n=30 3 [0-4.3]	0.086	n=43 5 [4-5]	n=42 5 [4-5]	0.134
Motricity[9] Index median [IQR]	n=36	n=29		n=43	n=42	
Arm	53 [15-77]	77 [35-93]	**0.039**	100[85-100]	100[86-100]	0.544
Leg	73 [48.8-92]	76 [41-85]	0.899	100[92-100]	100[81-100]	0.792
Total	67 [44-76.5]	76.5[41.5-86.5]	0.204	100[88-100]	100[84.8-100]	0.938
Star cancellation test[79, 80] fail n (%)	n=37 15 (41%)	n=30 15 (50%)	0.469	n=43 10 (23%)	n=42 3 (7%)	0.068
Shoulder Shrug Test[71] median [IQR]	n=36 1 [0.3-2]	n=29 2 [1-2]	0.115	n=43 2 [2-2]	n=42 2 [2-2]	0.858
Upper arm girth[133] in cm median [IQR]	n=36 29 [26.3-33]	n=30 30 [29-35.3]	0.087	n=43 32 [29-36]	n=42 33 [31-35]	0.543

No statistically significant differences between the groups were seen on any of the upper limb outcome measures for participants who scored more than 0 on the ARAT[6, 7] at the initial assessment (Table 22).

There were no statistically significant differences in the affected upper limb pain assessment[127, 128, 130, 131] at 3 months when this was analysed according to initial arm function (Table 23).

Table 23: 3-month upper limb pain (affected side) [127, 128, 130, 131], according to initial arm function

	Intervention	Control	P value	Intervention	Control	P value
	ARAT=0	ARAT=0		ARAT>0	ARAT>0	
Pain	n=37	n=30		n=43	n=42	
Affected side – n(%)	23 (62%)	19 (63%)	1.000	14 (33%)	14 (33%)	1.000
If Pain	n=23	n=19		n=14	n=14	
Severity scale – median [IQR]	2 [1.3]	3 [2-3]	0.220	3 [2-3.3]	3 [2-3.3]	0.839
Numerical rating scale – median [IQR]	6 [3-9]	7 [5-8]	0.557	6 [3.5-7.3]	5 [3.5-7.3]	0.874
Humeral lateral rotation – median [IQR]	n=37	n=30		n=43	n=42	
Passive	70 [52-95]	82.5 [64.8-94]	0.340	95 [86-110]	92 [80-100]	0.131
Active	50 [10-82.5]	62.5 [0-86.3]	0.765	85 [70-100]	82 [63.8-100]	0.478

Table 24: Disability and global health status, according to initial arm function

	Intervention	Control	P value	Intervention	Control	P value
	ARAT=0	ARAT=0		ARAT>0	ARAT>0	
Nottingham-EADL Index[110]	n=37	n=30		n=43	n=41	
median [IQR]						
Mobility	0 [0-1]	0 [0-2.3]	0.576	4 [1-6]	4 [2-6]	0.645
Kitchen	1 [0-3.5]	0 [0-5]	0.661	5 [3-5]	4 [2-5]	0.532
Domestic	0 [0-0.5]	0 [0-1.3]	0.569	1 [1-5]	1 [1-3.5]	0.773
Leisure	1 [0-2]	1 [0-2.3]	0.638	3 [2-4]	3 [2-3]	0.874
Total	2 [0.5-7]	2 [0-13]	0.959	11.0 [8-18.0]	12 [7.5-16.5]	0.717
NHP[116]	n=33	n=29		n=43	n=41	
median [IQR]						
Energy level	60.8[24-100]	60.8[24-63.2]	0.554	36.8[24-100]	60.8[24-100]	0.376
Pain	22.9[0-60.4]	20.5[0-52]	0.865	9[0-34.6]	14.8[0-37.5]	0.347
Emotional reactions	27.3[7.1-61.8]	21[7.2-49.7]	0.461	16.8[0-45.8]	16.4[3.5-43.1]	0.636
Sleep	49.6[12.6-77.6]	12.6[0-55.3]	0.142	22.4[0-77.6]	12.6[0-34.3]	0.308
Social Isolation	22[0-44.5]	0[0-22.5]	0.324	0[0-22.5]	0[0-44.1]	0.440
Physical abilities	47.6[32.2-65.2]	56.1[32.3-64.6]	0.908	32.8[0-56]	34.5[11.2-54.9]	0.481
Total	40.7[20.5-59.8]	28.9[15.8-52.8]	0.259	27.7[6.1-45.5]	28.6[16.2-47.7]	0.569

Assessment of disability using the Nottingham EADL Index[110], and global health status using the Nottingham Health Profile (NHP)[116] showed no statistically significant differences between the groups at 3 months when the results were analysed according to initial arm function (Table 24).

5.2 Further exploratory analyses

Further exploratory analyses were undertaken. As the results of our single pre-planned subgroup analysis showed that the negative effect of sNMES was only seen in those with initially severe upper limb impairment, we chose other subgroups which were measures of stroke severity: the presence or absence of shoulder weakness at baseline (measured by the Shoulder Shrug Test[71]), the NIHSS[197], and the stroke subtype (TACS/PACS vs. LACS/POCS)[198].

We also hypothesised that the side of deficit may be of importance. Those with the non-dominant arm affected and/or those with visuospatial deficit (seen more commonly in right hemisphere strokes) may have been more susceptible to any negative effects of sNMES. Those with sensory deficits may also have been more susceptible.

1. Other measures of stroke severity
    - Initial Shoulder Shrug Test[71] (score 0 vs. score 1 or 2) as there is evidence that the presence of a shoulder shrug following stroke is a good prognostic indicator for recovery of hand movement[72].
    - National Institute of Health Stroke Scale (binary split of initial NIHSS score i.e. 0-9 vs. >/=10)[197]
    - Stroke subtype (TACS/PACS vs. LACS/POCS)[198]
2. Side of upper limb impairment (left versus right)
3. Dominant hand versus non-dominant hand affected
4. Presence/absence of visuospatial deficit at baseline
5. Presence/absence of sensory loss at baseline

Change from baseline was also analysed.

5.2.1 Outcomes according to initial Shoulder Shrug Test

In those with moderate/severe shoulder weakness at baseline (Shoulder Shrug Test[71] score 0 or 1), arm function as measured by the total ARAT[6, 7] score at 3 months was statistically

significantly better in the control group than the intervention group. With respect to the other measures of upper limb impairment and disability at 3 months, differences were also seen in favour of the control group and these reached statistical significance in the grasp, grip and gross subsections of the ARAT[6, 7], the FAT[8] and the Arm Motricity Index[9] (Table 25).

Table 25: 3-month upper limb outcomes (affected side), according to initial Shoulder Shrug Test[71]

	Intervention	Control	P value	Intervention	Control	P value
	Shoulder Shrug=0-1 N=58	Shoulder Shrug=0-1 n=54		Shoulder Shrug=2 n=21	Shoulder Shrug=2 n=20	
ARAT[6, 7] median [IQR]	33 [0-57]	54 [30-57]	**0.046**	57 [47.5-57]	58 [51-57]	0.859
Grasp	6 [0-18]	18 [4.5-18]	**0.022**	18 [13.5-18]	18 [18-18]	0.234
Grip	12 [0-12]	12 [2.3-12]	**0.077**	12 [12-12]	12 [12-12]	0.582
Pinch	6 [0-18]	16 [0-18]	0.104	18 [15-18]	18 [13-18]	0.975
Gross	9 [0-9]	9 [6.8-9]	**0.023**	9 [9-9]	9 [9-9]	0.299
FAT[8] median [IQR]	3 [0-5]	4 [2-5]	**0.014**	5 [4-5]	5 [4.3-5]	0.455
Motricity[9] Index median [IQR]						
Arm	77 [43.8-94.8]	89 [77-100]	**0.018**	100 [88.5-100]	100 [93-100]	0.683
Leg	84 [64-100]	84 [61.5-100]	0.993	100 [92-100]	100 [86-100]	0.899
Total	76.5 [48.9-97]	84.5 [69.3-100]	0.210	100 [90.5-100]	100 [90.4-100]	0.793

In those with no shoulder weakness at baseline (Shoulder Shrug Test[71] score 2), no statistically significant differences were seen between groups at 3 months in terms of arm function, disability and impairment as measured by the ARAT[6, 7], FAT[8] and Motricity Index[9] (Table 25). However, the numbers in these groups were small, and there may have been a ceiling effect as all of the scores were at the top end of the ranges.

5.2.2 Outcomes according to NIHSS

In those with less severe strokes (NIHSS[197] 0-9), the control group achieved statistically significantly higher scores in the grasp and gross subsections of the ARAT[6, 7], and the FAT at 3 months than the intervention group (Table 26).

Table 26: 3-month upper limb outcomes (affected side), according to NIHSS[197]

	Intervention	Control	P value	Intervention	Control	P value
	Initial NIH score 0-9 n=49	Initial NIH score 0-9 n=47		Initial NIH score >/=10 n=30	Initial NIH score >/=10 n=27	
ARAT[6, 7] median [IQR]	57 [30-57]	57 [51-57]	0.181	0 [0-40.5]	33 [0-54]	0.167
Grasp	18 [6-18]	18 [18-18]	**0.006**	0 [0-12.8]	10 [0-18]	0.244
Grip	12 [12-12]	12 [12-12]	0.171	0 [0-12]	9 [0-12]	0.137
Pinch	18 [6-18]	18 [15-18]	0.293	0 [0-12]	0 [0-17]	0.405
Gross	9 [9-9]	9 [9-9]	**0.048**	0 [0-9]	9 [0-9]	0.099
FAT[8] median [IQR]	n=50 5 [3-5]	n=47 5 [4-5]	**0.011**	n=30 0 [0-4]	n=28 3 [0-4]	0.107
Motricity[9] Index median [IQR]	n=49	n=47		n=30	n=27	
Arm	93 [77-100]	100 [86-100]	0.056	53 [7.8-81.5]	77 [30-100]	0.125
Leg	100 [76-100]	100 [77.5-100]	0.719	76 [38-100]	76 [34-86]	0.728
Total	96 [76.5-100]	96.3 [84.4-100]	0.383	67.5 [36.4-88.1]	76.5 [39-89]	0.391

In those with more severe strokes (NIHSS[197] >/=10), absolute differences were seen in favour of the control group at 3 months in terms of arm function, disability and impairment as measured by the total ARAT[6, 7], grasp, grip and gross subsections of the ARAT[6, 7], FAT[8] and Arm Motricity Index[9] (Table 26). None of these differences reached statistical significance but the numbers in both of these groups were small.

5.2.3 Outcomes according to stroke subtype

Table 27: 3-month upper limb outcomes (affected side), according to stroke subtype[198]

	Intervention	Control	P value	Intervention	Control	P value
	TACS/PACS n=46	TACS/PACS n=37		LACS/POCS n=33	LACS/POCS n=37	
ARAT[6, 7] median [IQR]	34 [0-57]	43 [10.5-57]	0.573	54 [17.5-57]	57 [52.5-57]	**0.043**
Grasp	6 [0-18]	18 [0-18]	0.226	18 [5.5-18]	18 [16.5-18]	**0.024**
Grip	12 [0-12]	12 [0-12	0.693	12 [2.5-12]	12 [0-12]	**0.019**
Pinch	6 [0-18]	12 [0-18]	0.686	18 [6-18]	18 [13.5-18]	0.139
Gross	9 [0-9]	9 [2-9]	0.221	9 [4-9]	9 [9-9]	**0.035**
FAT[8] median [IQR]	n=46 3.5 [0-5]	n=38 4 [1.5-5]	0.474	n=34 4 [2-5]	n=37 5 [4-5]	**0.003**
Motricity[9] Index median [IQR]						
Arm	77 [46.5-100]	92 [76-100]	0.417	85 [70-100]	100 [84.5-100]	**0.016**
Leg	92 [57.5-100]	84 [70-100]	0.977	92 [76-100]	92 [76-100]	0.936
Total	86 [46.8-100]	88 [71.5-100]	0.671	88 [70.8-100]	92 [80.6-100]	0.223

In those with lacunar strokes (LACS) or posterior circulation strokes (POCS) i.e. no disturbance of higher cortical dysfunction, the control group achieved statistically significantly

higher scores at 3 months in the total ARAT[6, 7], grasp, grip and gross subsections of the ARAT[6, 7], FAT and Arm Motricity Index[9] than the intervention group (Table 27).

In those with total or partial anterior circulation strokes (TACS or PACS), differences were seen in favour of the control group at 3 months in the total ARAT[6, 7], grasp and pinch subsections of the ARAT[6, 7] and Arm Motricity Index[9] (Table 27). None of these differences reached statistical significance.

5.2.4 Outcomes according to side of upper limb impairment

There were statistically significant differences in favour of the control group in the grasp and gross subsections of the ARAT[6, 7] in those participants with left sided impairment. In these subjects, arm function as measured by the total ARAT[6, 7] score at 3 months, was also better in the control group but the difference did not reach statistical significance (Table 28).

In terms of the other measures of upper limb impairment and disability (the FAT[8] and the Arm Motricity Index[9]), there were differences in favour of the control group in those with left sided impairment but these differences did not reach statistical significance (Table 28).

Table 28: 3-month upper limb outcomes (affected side), according to side of upper limb impairment

	Intervention	Control	P value	Intervention	Control	P value
Side of impairment	Left	Left		Right	Right	
ARAT[6, 7] median [IQR]	n=53	n=45		n=26	n=29	
Total	33 [0-57]	54 [27-57]	0.124	55.5 [31.3-57]	57 [43-57]	0.480
Grasp	6 [0-18]	18 [3-18]	**0.044**	18 [6-18]	18 [13.5-18]	0.263
Grip	12 [0-12]	12 [3-12]	0.129	12 [8.8-12]	12 [12-12]	0.511
Pinch	6 [0-18]	17 [0-18]	0.240	18 [5.3-18]	18 [12-18]	0.618
Gross	9 [0-9]	9 [8-9]	**0.047**	9 [6.8-9]	9 [9-9]	0.310
FAT[8] median [IQR]	n=54 3.5 [0-5]	n=45 4 [2.5-5]	0.065	n=26 4.5 [2-5]	n=30 5 [4-5]	0.176
Motricity[9] Index median [IQR]	n=53	n=44		n=26	n=30	
Arm	78 [46.5-100]	92.5 [77-100]	0.142	85 [70-100]	96.5 [84-100]	0.093
Leg	92 [64-100]	85 [70-100]	0.961	92 [76-100]	100 [76-100]	0.900
Total	86 [48.3-100]	88.5 [84-100]	0.440	88 [73.1-100]	93 [76.5-100]	0.488

The median total ARAT[6, 7] score at 3 months in those with right sided impairment was also greater in the control group but, again, this difference did not reach statistical significance. In these subjects, there were also differences in favour of the control group in terms of other measures of upper limb impairment and disability (the FAT[8] and the Arm Motricity Index[9]), but these were not statistically significant (Table 28).

5.2.5 Outcomes according to whether or not dominant hand affected

In those with the non-dominant hand affected, the control group achieved statistically significantly higher scores at 3 months in the total ARAT[6, 7], grasp and gross subsections of the ARAT[6, 7], FAT and Arm Motricity Index[9] than the intervention group (Table 29).

In those with the dominant hand affected, small absolute differences were seen in favour of the control group at 3 months in the total ARAT[6, 7] and Arm Motricity Index[9] but these did not reach statistical significance (Table 29). The numbers in these groups were small and the subjects may have had less severe strokes as many individuals were excluded because of dysphasia. There may have been a ceiling effect as all of the scores were at the top end of the ranges.

Table 29: 3-month upper limb outcomes (affected side), according to whether or not dominant hand affected

	Intervention	**Control**	**P value**	**Intervention**	**Control**	**P value**
	Dominant hand affected n=25	Dominant hand affected n=26		Non-dominant hand affected n=53	Non-dominant hand affected n=47	
ARAT[6, 7] median [IQR]	57 [40-57]	57 [43-57]	0.925	30 [0-57]	54 [24-57]	**0.043**
Grasp	18 [9-18]	18 [14.3-18]	0.787	6 [0-18]	18 [1.5-18]	**0.014**
Grip	12 [12-12]	12 [12-12]	0.913	12 [0-12]	12 [3.8-12]	0.056
Pinch	18 [13.5-18]	18 [12-18]	0.830	6 [0-18]	16.5 [0-18]	0.110
Gross	9 [9-9]	9 [9-9]	0.610	9 [0-9]	9 [7.5-9]	**0.020**
FAT[8]	n=26	n=27		n=54	n=48	
median [IQR]	5 [3-5]	5 [4-5]	0.677	3 [0-5]	4.5 [2.3-5]	**0.013**
Motricity[9] Index	n=26	n=27		n=53	n=47	
median [IQR]						
Arm	92 [77-100]	100 [84-100]	0.338	77 [46.5-100]	92 [77-100]	**0.049**
Leg	100 [76-100]	100 [76-100]	0.704	92 [64-100]	84 [70-100]	0.786
Total	96 [75.5-100]	94.5 [76.5-100]	0.977	84 [48.3-100]	88.5 [76.5-100]	0.225

5.2.6 Outcomes according to presence/absence of visuospatial deficit at baseline

In those with no visuospatial deficit at baseline, the control group achieved statistically significantly higher scores than the intervention group at 3 months in the following measures of arm function, disability and impairment: total ARAT[6, 7], grasp, grip and gross subsections of the ARAT[6, 7], FAT and Arm Motricity Index[9] (Table 30).

Table 30: 3-month upper limb outcomes (affected side), according to presence/absence of visuospatial deficit at baseline

	Intervention	Control	P value	Intervention	Control	P value
	Visuospatial deficit at baseline n=40	Visuospatial deficit at baseline n=23		No visuospatial deficit at baseline n=39	No visuospatial deficit at baseline n=51	
ARAT[6, 7] median [IQR]	24.5 [0-57]	33 [0-54]	0.682	54 [26-57]	57 [51-57]	**0.067**
Grasp	6 [0-18]	12 [0-18]	0.988	18 [6-18]	18 [18-18]	**0.010**
Grip	8.5 [0-12]	7 [0-12]	0.752	12 [5-12]	12 [12-12]	**0.045**
Pinch	3 [0-18]	0 [0-17]	0.403	18 [6-18]	18 [15-18]	0.126
Gross	7.5 [0-9]	9 [0-9]	0.866	9 [7-9]	9 [9-9]	**0.019**
FAT[8]	n=40	n=23		n=40	n=52	
median [IQR]	3 [0-5]	3 [0-4]	0.720	4 [2.3-5]	5 [4-5]	**0.004**
Motricity[9] Index	n=39	n=22		n=40	n=52	
median [IQR]						
Arm	77 [40-100]	77 [29.8-100]	0.866	92 [77-100]	100 [84.3-100]	**0.039**
Leg	92 [48-100]	76 [33.8-100]	0.451	92 [76-100]	100 [76-100]	0.835
Total	76 [44-100]	77 [29.5-100]	0.903	90.5 [73.6-100]	92 [81-100]	0.309

In those with visuospatial deficit at baseline, absolute differences were seen in favour of the control group at 3 months in the total ARAT[6, 7] and grasp and gross subsections of the ARAT[6, 7] but these did not reach statistical significance (Table 30). The numbers in these groups were small.

5.2.7 Outcomes according to presence/absence of sensory loss at baseline

In those with no sensory loss at baseline, the control group achieved statistically significantly higher scores at 3 months in the total ARAT[6, 7], grasp, grip and gross subsections of the ARAT[6, 7], FAT and Arm Motricity Index[9] than the intervention group (Table 31).

For those with sensory loss at baseline, absolute differences were seen in favour of the control group at 3 months in the total ARAT[6, 7], grasp and pinch subsections of the ARAT[6, 7], and Arm Motricity Index[9] but these did not reach statistical significance (Table 31). The numbers in these groups were small.

Table 31: 3-month upper limb outcomes (affected side), according to presence/absence of sensory loss at baseline

	Intervention	Control	P value	Intervention	Control	P value
	Sensory loss at baseline n=36	Sensory loss at baseline n=32		No sensory loss at baseline n=43	No sensory loss at baseline n=42	
ARAT[6, 7] median [IQR]	36.5 [0-57]	48.5 [5.3-57]	0.689	51 [8-57]	57 [42.8-57]	**0.027**
Grasp	9.5 [0-18]	18 [0-18]	0.338	15 [4-18]	18 [14.3-18]	**0.013**
Grip	12 [0-12]	12 [0-12]	0.573	12 [0-12]	12 [12-12]	**0.045**
Pinch	6 [0-18]	13.5 [0-18]	0.821	17 [0-18]	18 [12-18]	0.071
Gross	9 [0-9]	9 [1-9]	0.267	9 [2-9]	9 [9-9]	**0.022**
FAT[8]	n=36	n=33		n=44	n=42	
median [IQR]	3.5 [0-5]	4 [1-5]	0.224	4 [2-5]	5 [4-5]	**0.024**
Motricity[9] Index	n=36	n=33		n=43	n=41	
median [IQR]						
Arm	77 [45.8-100]	86 [77-100]	0.355	85 [71-100]	100 [84-100]	**0.024**
Leg	92 [54.3-100]	80 [71.5-100]	0.667	92 [70-100]	100 [76-100]	0.722
Total	84 [47.6-100]	83.3 [65.5-96.5]	0.771	88.5 [68.5-100]	92 [77-100]	0.178

5.2.8 Change from initial assessment

5.2.8.1 Change from initial to 4-week assessment

There were no statistically significant differences between the groups in any of the upper limb outcome measures when assessing the change from the initial to the 4-week assessment (i.e. upper limb impairment and disability (ARAT[6, 7], FAT[8], Motricity Index[9], Star Cancellation Test[79], and Shoulder Shrug Test[71]), and upper arm girth[133]) (Table 32). In terms of upper limb function, the median ARAT[6, 7] gain was 3.5 and 1 in the intervention and control groups respectively. Clinically, this reflects an improvement from not being able to do a subtest and then to partially complete it, or being able to partially do a subtest and then complete it fully. Median FAT[8] gains were 0 and 1 in the intervention and control groups respectively. The FAT[8] consists of 5 tasks and is scored from 0 to 5. Clinically, a gain of 1 indicates the ability to complete a task that could not be done previously.

Table 32: 4-week upper limb outcome measures (affected side) - change from initial to 4-week assessment

	Intervention (n=83)	Control (n=82)	P value
ARAT[6, 7] change median [IQR]	n=80	n=79	
Total	3.5 [0-24.3]	1 [0-30]	0.602
Grasp	0 [0-7]	0 [0-9]	0.865
Grip	0 [0-7]	0 [0-6]	0.698
Pinch	0 [0-6]	0 [0-9]	0.725
Gross	0 [0-4]	0 [0-4]	0.482
FAT[8] change median [IQR]	n=83 0 [0-2]	n=82 1 [0-2]	0.920
Motricity[9] Index change median [IQR]	n=83	n=81	
Arm	14 [0-29]	21 [5-35.5]	0.137
Leg	9 [0-22]	8 [0-22]	0.986
Total	12.5 [0-24.5]	14.5 [4.3-27.3]	0.258
Star cancellation test[79, 80] change n (%)	n=83	n=82	
Baseline Fail – 4-week Fail	23 (28%)	21 (26%)	0.607*
Baseline Fail – 4-wk Pass	11 (13%)	7 (9%)	
Baseline Pass – 4-wk Fail	4 (5%)	7 (9%)	
Baseline Pass – 4-wk Pass	45 (54%)	47 (57%)	
Shoulder Shrug Test[71] change median [IQR]	n=83 0 [0-1]	n=81 0 [0-1]	0.162
Upper arm girth[133] (cm) change median [IQR]	n=75 1 [-1-2.5]	n=74 0 [-1.5-2.0]	0.366

* A chi square test on a 4x2 table was used (to show whether the distribution of the values in the cells is significantly different or not) therefore only one p value for the whole table.

Change in affected upper limb pain from the initial assessment to 4 weeks was also similar between groups in terms of presence of pain, severity of pain[127, 128], and pain-free range of humeral lateral rotation[130, 131] (Table 33).

Table 33: 4-week upper limb pain (affected side) [127, 128, 130, 131]- change from initial to 4-week assessment

	Intervention (n=83)	Control (n=82)	P value
Pain change n (%)			
Baseline no pain – 4-wk no pain	52 (63%)	47 (57%)	0.748*
Baseline no pain – 4-wk pain	11 (13%)	16 (20%)	
Baseline pain – 4-wk no pain	9 (11%)	9 (11%)	
Baseline pain – 4-wk pain	11 (13%)	10 (12%)	
Severity scale change – median [IQR]	0 [0-0]	0 [0-0.3]	0.900
Numerical rating scale change – median [IQR]	0 [0-0]	0 [0-0]	0.636
Humeral lateral rotation change – median [IQR]			
Passive	n=80 14.5 [-5-27.3]	n=79 10 [-15-34]	0.960
Active	n=81 -5 [-60-0]	n=77 -10 [-42.5-2]	0.822

* A chi square test on a 4x2 table was used (to show whether the distribution of the values in the cells is significantly different or not) therefore only one p value for the whole table.

5.2.8.2 Change from initial to 3-month assessment

The change in arm function (measured by the total ARAT[6, 7] and FAT[8]) from the initial to the 3-month assessment was greater in the control group than the intervention group but this difference did not reach statistical significance. There were, however, significant differences in favour of the control group in the grasp and gross subsections of the ARAT[6, 7] when analysing change from the initial to the 3-month assessment (Table 34). The gains in ARAT[6, 7] and FAT[8] scores in the intervention group were similar to those at 4 weeks, whereas those in the control group were greater, indicating further improvements in the controls between 4 weeks and 3 months.

In terms of change from the initial to the 3-month assessment for the other measures of upper limb impairment and disability (i.e. the Motricity Index[9], the Star Cancellation Test[79, 80], and Shoulder Shrug Test[71]), and upper arm girth[133], there were no statistically significant differences between the randomisation groups (Table 34).

Table 34: 3-month upper limb outcome measures (affected side) - change from initial to 3-month assessment

	Intervention (n=80)	Control (n=75)	P value
ARAT[6, 7] change median [IQR]	n=79	n=71	
Total	6.0 [0-30]	12 [0-43]	0.100
Grasp	0 [0-6]	3 [0-15]	**0.027**
Grip	0 [0-11]	3 [0-12]	0.197
Pinch	3 [0-9]	6 [0-13]	0.278
Gross	0 [0-3]	1 [0-7]	**0.025**
FAT[8] change median [IQR]	n=80 1 [0-2.8]	n=75 1 [0-4]	0.053
Motricity[9] Index change median [IQR]	n=79	n=74	
Arm	23 [1-37]	24 [9.8-47.3]	0.209
Leg	16 [8-27]	16 [0-29]	0.782
Total	19 [8.5-30.5]	17.5 [10-34.3]	0.483
Star cancellation[79, 80] change n (%)	n=80	n=75	
Baseline Fail – 3-month Fail	19 (24%)	13 (17%)	0.624
Baseline Fail – 3-month Pass	12 (15%)	9 (12%)	
Baseline Pass – 3-month Fail	6 (8%)	5 (7%)	
Baseline Pass – 3-month Pass	43 (54%)	48 (64%)	
Shoulder Shrug Test[71] change median [IQR]	n=79 0 [0-1]	n=74 1 [0-1]	0.226
Upper arm girth[133] (cm) change median [IQR]	n=73 -1 [-3.0-0.5]	n=70 0 [-2.0-2.0]	0.181

Change in affected upper limb pain from the initial to the 3-month assessment was similar between groups for presence of pain, severity of pain, and pain-free range of humeral lateral rotation[127, 128, 130, 131] (Table 35).

Table 35: 3-month upper limb pain (affected side)[127, 128, 130, 131] - change from initial to 3-month assessment

	Intervention (n=80)	Control (n=75)	P value
Pain change n (%)			
Baseline no pain – 3-month no pain	34 (43%)	31 (41%)	0.906
Baseline no pain – 3-month pain	27 (34%)	27 (36%)	
Baseline pain – 3-month no pain	9 (11%)	10 (13%)	
Baseline pain – 3-month pain	10 (13%)	7 (9%)	
Severity scale – median [IQR]	0 [-2.0-2.0]	0 [-2.0-0.0]	0.727
Numerical rating scale – median [IQR]	0.0 [0.0-4.0]	0.0 [0.0-5.0]	0.952
Humeral lateral rotation – median [IQR]			
Passive	-10 [-35-10]	-16 [-30-10]	0.788
Active	17.5 [0-58.8]	12 [-6-55]	0.476

5.2.9 Change from initial assessment, according to initial arm function

5.2.9.1 Change from initial to 4-week assessment

Table 36: 4-week upper limb outcome measures (affected side) - change from initial to 4-week assessment, according to initial arm function.

	Intervention (n=39)	Control (n=37)	P value	Intervention (n=43)	Control (n=42)	P value
	ARAT=0	ARAT=0		ARAT>0	ARAT>0	
ARAT[6, 7] change median [IQR]	n=37	n=37		n=43	n=42	
Total	0 [0-20.5]	0 [0-43]	0.917	7 [1-26]	3 [0-26.3]	0.405
Grasp	0 [0-7]	0 [0-12]	0.702	0 [0-8]	1 [0-9]	0.881
Grip	0 [0-4.5]	0 [0-12]	0.555	1 [0-7]	2 [0-6]	0.996
Pinch	0 [0-1.5]	0 [0-8.5]	0.520	3 [0-9]	0 [0-10]	0.409
Gross	0 [0-9]	0 [0-9]	0.844	0 [0-3]	0 [0-4]	0.447
FAT[8] change median [IQR]	n=39 0 [0-2]	n=37 0 [0-1]	0.702	n=43 1 [0-2]	n=42 1 [0-3]	0.900
Motricity Index[9] change median [IQR]	n=39	n=36		n=43	n=42	
Arm	14 [0-34]	31.5 [9.5-46.3]	**0.042**	13 [0-27]	13 [4-24]	0.772
Leg	14 [-2-23]	8 [-5.8-31.3]	0.941	8 [0-16]	9.5 [0-22]	0.901
Total	14.5 [-2-30.5]	21 [8.9-34]	0.110	12.5 [4-21.5]	11.5 [-0.3-23.5]	0.775
Star cancellation[79, 80] change n (%)	n=39	n=37		n=43	n=42	
Fail - Fail	17 (44%)	18 (49%)	0.507	5 (12%)	3 (7%)	0.771
Fail - Pass	6 (15%)	4 (11%)		5 (12%)	3 (7%)	
Pass - Fail	2 (5%)	5 (14%)		2 (5%)	2 (5%)	
Pass – Pass	14 (36%)	10 (27%)		31 (72%)	34 (81%)	
Shoulder Shrug Test[71] change median [IQR]	n=39 0 [0-1]	n=36 0 [0-1]	0.641	n=43 0 [0-1]	n=42 0 [0-1]	0.127
Upper arm girth[133] (cm) change median [IQR]	n=34 1.5 [0-3.0]	n=32 0 [-1.8-2.0]	0.120	n=41 1 [-1.8-2.0]	n=39 0 [-1.5-2.0]	0.954

The change from the initial to the 4-week assessment was also analysed according to initial arm function (i.e. ARAT=0 vs. ARAT>0). In the ARAT=0 group, the increase in Arm Motricity Index score from baseline to 4 weeks was statistically significantly greater in the control group than the intervention group. No other statistically significant differences were seen between groups on any of the upper limb outcome measures i.e. upper limb impairment and disability (ARAT[6, 7], FAT[8], Motricity Index[9], Star Cancellation Test[79, 80], and Shoulder Shrug Test[71]), and upper arm girth[133] (Table 36).

There were no statistically significant differences between groups for the affected upper limb pain assessment[127, 128, 130, 131] when analysing change from the initial to the 4-week assessment, according to initial arm function (Table 37).

Table 37: 4-week upper limb pain (affected side)[127, 128, 130, 131] - change from initial to 4-week assessment, according to initial arm function

	Intervention	Control	P value	Intervention	Control	P value
	ARAT=0	ARAT=0		ARAT>0	ARAT>0	
Pain change n (%)	n=39	n=37		n=43	n=42	
No pain – No pain	19 (49%)	18 (49%)	0.244	32 (74%)	27 (64%)	0.350
No pain – Pain	8 (21%)	13 (35%)		3 (7%)	3 (7%)	
Pain – No pain	3 (8%)	3 (8%)		6 (14%)	5 (12%)	
Pain – Pain	9 (23%)	3 (8%)		2 (5%)	7 (17%)	
Severity scale change– median [IQR]	n=39 0 [0-1]	n=37 0 [0-1.5]	0.516	n=43 0 [0-0]	n=42 0 [0-0]	0.793
Numerical rating scale change– median [IQR]	n=38 0 [-3-0]	n=36 0 [-3.5-0]	0.435	n=43 0 [0-0]	n=42 0 [0-0]	0.955
Humeral lateral rotation change– median [IQR]						
Passive	n=37 20 [12.5-35.5]	n=34 28 [-2.5-4.7]	0.913	n=43 0 [-35-15]	n=42 0 [-16.3-20]	0.579
Active	n=37 -10 [-60-0]	n=32 -40 [-65.8-0]	0.401	n=43 -5 [-45-10]	n=42 -3.5 [-20-26.3]	0.309

5.2.9.2 Change from initial to 3-month assessment

The change from the initial to the 3-month assessment was analysed according to initial arm function (ARAT=0 vs. ARAT>0).

Differences were seen in favour of the control group when analysing participants who scored 0 on the ARAT[6, 7] initially (Table 38). The control group achieved greater improvements in arm function as measured by the FAT[8] and Arm Motricity Index[9], and this difference in the Arm Motricity Index scores reached statistical significance. For the ARAT=0 group, no

significant differences were seen in the other measures of upper limb impairment and disability (i.e. the Star Cancellation Test[79, 80] and Shoulder Shrug Test[71]), and measurement of upper arm girth[133] (Table 38).

For those participants scoring more than 0 on the ARAT[6, 7] at the initial assessment, no statistically significant differences were seen between randomisation groups on any of the upper limb outcome measures when analysing change from the initial assessment (Table 38).

Table 38: 3-month upper limb outcome measures (affected side) - change from initial to 3-month assessment, according to initial ARAT[6, 7] score

	Intervention	Control	P value	Intervention	Control	P value
	ARAT=0	ARAT=0		ARAT>0	ARAT>0	
ARAT[6, 7] change median [IQR]	n=37	n=30		n=42	n=41	
Total	0 [0-33.5]	34.5 [0-54]	0.057	9 [2-26.5]	10 [1.5-33.5]	0.788
Grasp	0 [0-6]	11 [0-18]	**0.049**	0.5 [0-8]	2 [0-12]	0.246
Grip	0 [0-12]	9.5 [0-12]	0.124	1 [0-10]	2 [0-7]	0.743
Pinch	0 [0-6]	3 [0-17.3]	0.179	5.5 [0-9]	6 [0-12]	0.876
Gross	0 [0-9]	9 [0-9]	**0.034**	0 [0-2]	0 [0-3.5]	0.129
FAT[8] change median [IQR]	n=37 0.0 [0-3]	n=30 2.5 [0-4.3]	0.065	n=43 1.0 [0-2]	n=42 1.0 [0-4]	0.268
Motricity[9] Index change median [IQR]	n=36	n=29		n=43	n=42	
Arm	28.5 [0-42.8]	47 [15.5-72.5]	**0.027**	23 [7-27]	16 [8-27.3]	0.771
Leg	23.5 [0-27)	17 [0-34]	0.921	16 [8-24]	16 [8-27]	0.860
Total	20 [10.8-30.9]	31 [9-45.5]	0.122	15 [8-29]	13 [10-26.8]	0.932
Star cancellation[79, 80] test change n(%)	n=37	n=30		n=43	n=32	
Fail - Fail	13 (35%)	12 (40%)	0.831	6 (14%)	1 (2%)	0.188
Fail - Pass	8 (22%)	5 (17%)		4 (9%)	4 (10%)	
Pass - Fail	2 (5%)	3 (10%)		4 (9%)	2 (5%)	
Pass – Pass	14 (38%)	10 (33%)		29 (67%)	35 (83%)	
Shoulder Shrug Test[71] change median [IQR]	n=36 0 [0-1]	n=29 1 [0-1]	0.155	n=43 0 [0-1]	n=42 0.5 [0-1]	0.637
Arm girth[133] (cm) change median [IQR]	n=32 -0.8 [-3.0-0.0]	n=28 0.0 [-3.0-2.0]	0.282	n=41 -1.0 [-2.0-0.5]	n=39 0.0 [-2.0-2.0]	0.492

There were also no statistically significant differences between groups for the affected upper limb pain assessment[127, 128, 130, 131] at 3 months when analysing change from baseline, according to initial arm function (Table 39).

Table 39: 3-month upper limb pain (affected side) [127, 128, 130, 131]- change from initial to 3-month assessment, according to initial arm function

	Intervention	Control	P value	Intervention	Control	P value
	ARAT=0	ARAT=0		ARAT>0	ARAT>0	
Pain change n (%)	n=37	n=30		n=43	n=42	
No pain – No pain	9 (24%)	10 (33%)	0.384	25 (58%)	20 (48%)	0.598
No pain – Pain	17 (46%)	16 (53%)		10 (23%)	10 (24%)	
Pain – No pain	5 (14%)	1 (3%)		4 (9%)	8 (19%)	
Pain – Pain	6 (16%	3 (10%)		4 (9%)	4 (10%)	
Change in Severity scale – median [IQR]	-1 [-2-0]	-1 [-2-0]	0.943	0 [-1-0]	0 [-1-0]	0.515
Numerical rating scale – median [IQR]	2 [0-5]	2 [0-7]	0.476	0 [0-1.0]	0 [-0.3-2]	0.520
Humeral lateral rotation – median [IQR]						
Passive	-30 [-40- -4]	-25 [-38.5- -3.8]	0.622	0 [-15-20]	-10 [-21.3-14.3]	0.205
Active	40 [0-60]	40 [0-80.5]	0.755	5 [-20-45]	0 [-30-20.5]	0.221

5.3 Summary of secondary analysis

- There were more dropouts between 4 weeks and 3 months in the control group than the intervention group. These dropouts were less impaired than the dropouts in the intervention group at 4 weeks, achieving higher scores on the ARAT[6, 7], FAT[8] and Arm Motricity Index[9].
- In the analysis of absolute outcomes at 3 months according to initial ARAT[6, 7] score, those in the control group with an initial ARAT[6, 7] of 0 achieved statistically significantly higher scores on the grasp and gross subsections of the ARAT and the Arm Motricity Index than those in the intervention group. These significant differences were not seen in those scoring more than 0 in the ARAT[6, 7] at baseline.
- Other measures of stroke severity:
  i. In those with moderate to severe shoulder weakness at baseline (Shoulder Shrug Test = 0 or 1), the control group achieved statistically significantly higher scores than the intervention group in the following outcome measures: total ARAT[6, 7], grasp, grip and gross subsections of the ARAT[6, 7], FAT[8] and Motricity Index[9]. These differences between groups were not seen in those with no initial shoulder weakness.
  ii. In those with less severe strokes (NIHSS[197] 0-9), the control group achieved statistically significantly higher scores than the intervention group in the grasp and gross subsections of the ARAT[6, 7], and the FAT[8] at 3 months. Similar differences were seen in favour of the controls in those with more severe strokes (NIHSS[197] >/=10) but these did not reach statistical significance.
  iii. In those with LACS or POCS, the control group achieved statistically significantly higher scores than the intervention group at 3 months in the total ARAT[6, 7], the grasp, grip and gross subsections of the ARAT[6, 7], FAT[8] and Arm Motricity Index[9]. Again, differences were seen in favour of the control group in those with TACS or PACS but none reached statistical significance.
- In the analysis of results according to side of upper limb impairment, those participants in the control group with left sided impairment scoring 0 on the ARAT[6, 7] at baseline, achieved statistically significantly higher scores than the intervention group on the grasp and gross subsections of the ARAT[6, 7] at 3 months.
- In those with the non-dominant hand affected, the control group achieved statistically significantly higher scores than the intervention group at 3 months in the total ARAT[6, 7], the grasp and gross subsections of the ARAT[6, 7], FAT[8] and Arm Motricity Index[9]. Differences in favour of the control group in those with the dominant hand affected did not reach statistical significance.

- In those with no visuospatial deficit at baseline, the controls achieved statistically significantly higher scores than the intervention group at 3 months in the total ARAT[6, 7], the grasp, grip and gross subsections of the ARAT[6, 7], FAT[8] and Arm Motricity Index[9].
- In those with no sensory loss at baseline, the control group achieved statistically significantly higher scores than the intervention group at 3 months in the total ARAT[6, 7], the grasp, grip and pinch subsections of the ARAT[6, 7], FAT[8] and Arm Motricity Index[9].
- Differences were seen between groups in favour of the control group in those with visuospatial deficit and in those with sensory loss at baseline, but none of these differences reached statistical significance.
- In the ARAT=0 group, the increase in Arm Motricity Index[9] score from baseline to 4 weeks was statistically significantly greater in the control group than the intervention group.
- In the analysis of change from baseline to 3 months, the control group achieved statistically significantly higher scores on the grasp and gross subsections of the ARAT[6, 7].
- When analysing change from baseline to 3 months according to initial ARAT[6, 7] score, significantly higher scores in the control group were seen for those participants scoring 0 on the ARAT[6, 7] at baseline. In this subgroup, the change in Arm Motricity Index was also statistically significantly greater in the control group than those in the intervention group. However, no statistically significant results were seen when analysing the change from baseline to 3 months in those scoring greater than 0 in the ARAT[6, 7] at baseline.

Chapter 6 Compliance with Treatment

6.1 Compliance with treatment

Previous studies of electrical stimulation have described the participants' intended amount of stimulation. However, only two studies[152, 167] reported the amount of stimulation actually received.

Peurala et al[167] looked at the use of ES to both the upper and lower limbs to enhance sensorimotor recovery in chronic stroke. It was intended that participants receive 20-minute sessions twice daily (i.e. 14 sessions per week) for a 3-week period (i.e. a total of 42 sessions). Sham treatment was given to the control group. The authors reported that participants received a mean of 21.6 +/- 6 sessions in total but do not state whether there were any differences between the intervention and control groups. It is also unclear how many of the sessions received lasted for the full 20 minutes. No reasons were given for non-receipt of treatment.

Powell et al[152] looked at electrical stimulation to wrist extensors and intended that participants received 30 minutes of stimulation 3 times daily for 8 weeks. They monitored compliance using a diary and report that 19 participants (out of the 27 receiving ES) complied well, 3 missed occasional treatment sessions, and 5 complied poorly. Good compliance was not defined. Poor compliance was defined as receiving less than 50% of intended sessions.

In the current study, the treatment sessions were recorded in the participants' diaries by documenting the start and finish times. The diaries were also used to record reasons for non-receipt of treatment. They were completed by nursing staff or by the participants and carers. It was intended that all participants receive the full four-week course of treatment as prescribed i.e. 82 sessions (total of 76 hours). Participants received less than the intended stimulation either because the treatment was stopped early, or because individual sessions were missed, or both. When analysing the diaries, the number of hours given was looked at, rather than the number of sessions. Sessions where only one of the start or stop times was documented, and sessions left blank in the diary, were recorded as 'missed' sessions. Three of the diaries were lost (i.e. not returned at the 3-month assessment), therefore 173 were analysed.

The actual time (hours) that the sNMES was given as documented in the diaries is shown in Table 40. The maximum actually received in both groups was greater than the maximum prescribed time of 76 hours. This was because the stimulator was occasionally left on for longer than the prescribed session. For all the planned 60 minute sessions with times recorded, the actual time given varied from 5 minutes to 320 minutes. Further analysis of this shows that out of the 8051 recorded 60-minute sessions, 7531 (94%) were given for 60 minutes, 326 (4%) were for less than 60 minutes, and 194 (2%) were for more than 60 minutes. As shown in Table 40, the amount of sNMES actually received was similar between randomisation groups.

Table 40: Surface NMES received (actual time in hours)

	Intervention (n=87)	Control (n=86)	All (n=173)
Mean	51.6	51.0	51.3
Standard deviation	20.1	21.7	20.9
Minimum	1.0	0.5	0.5
Maximum	76.2	78.1	78.1
Median [IQR]	55.6 [43.3-68.3]	55.0 [39-70.2]	55.5 [39.8-69.1]

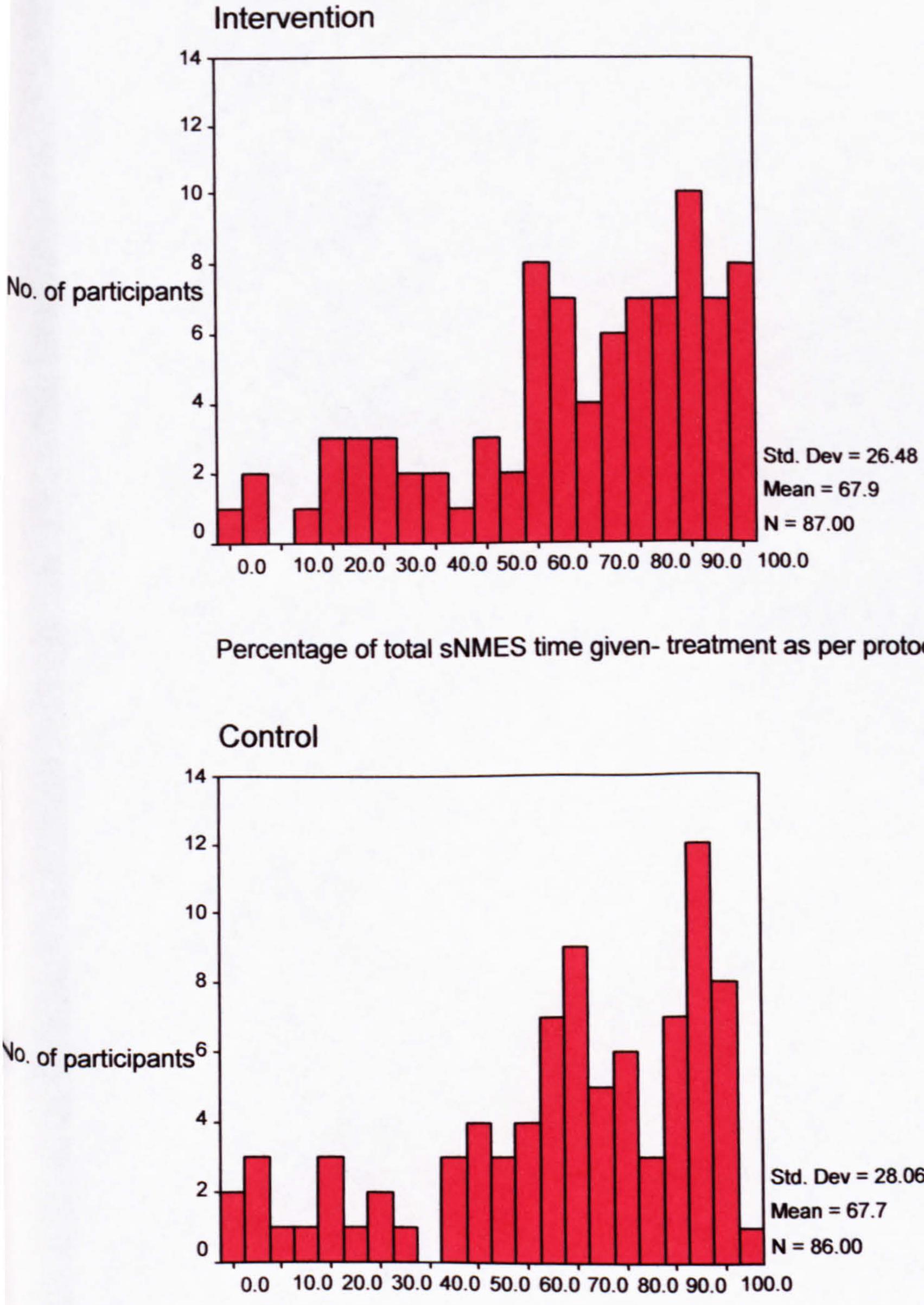
The overall diary data was then analysed in two ways: 'treatment as per protocol' and 'treatment as prescribed'. In the 'treatment as per protocol' analysis, all participants should have received the full 28 day treatment (i.e. 76 hours) unless they died during the treatment period. In the 'treatment received as prescribed' analysis, the amount of sNMES given was analysed as a percentage of sNMES prescribed.

In the 'treatment as per protocol', the participants received, on average, 67.8% of the intended 76 hours of stimulation, and this was similar between randomisation groups (Table 41 and Figure 8).

Table 41: Percentage of total sNMES given (treatment as per protocol)

	Intervention (n=87)	Control (n=86)	All (n=173)
Mean	67.91	67.7	67.81
Standard deviation	26.48	28.06	27.20
Minimum	1.32	0.66	0.66
Maximum	100.22	102.79	102.79
Median [IQR]	73.1 [56.95-89.91]	72.4 [52.8-92.38]	73 [53.95-90.89]

Figure 8: Histograms showing percentage of total sNMES given (treatment as per protocol)



In the 'treatment received as prescribed' analysis, we analysed compliance with treatment prescribed. The course of sNMES was discontinued early in some cases as discussed below and, in these cases, the sNMES was not prescribed for the total 76 hours.

Compliance with treatment prescribed was 76% overall, and similar between randomisation groups (Figure 9 and Table 42).

Figure 9: Histograms showing percentage of sNMES received as prescribed

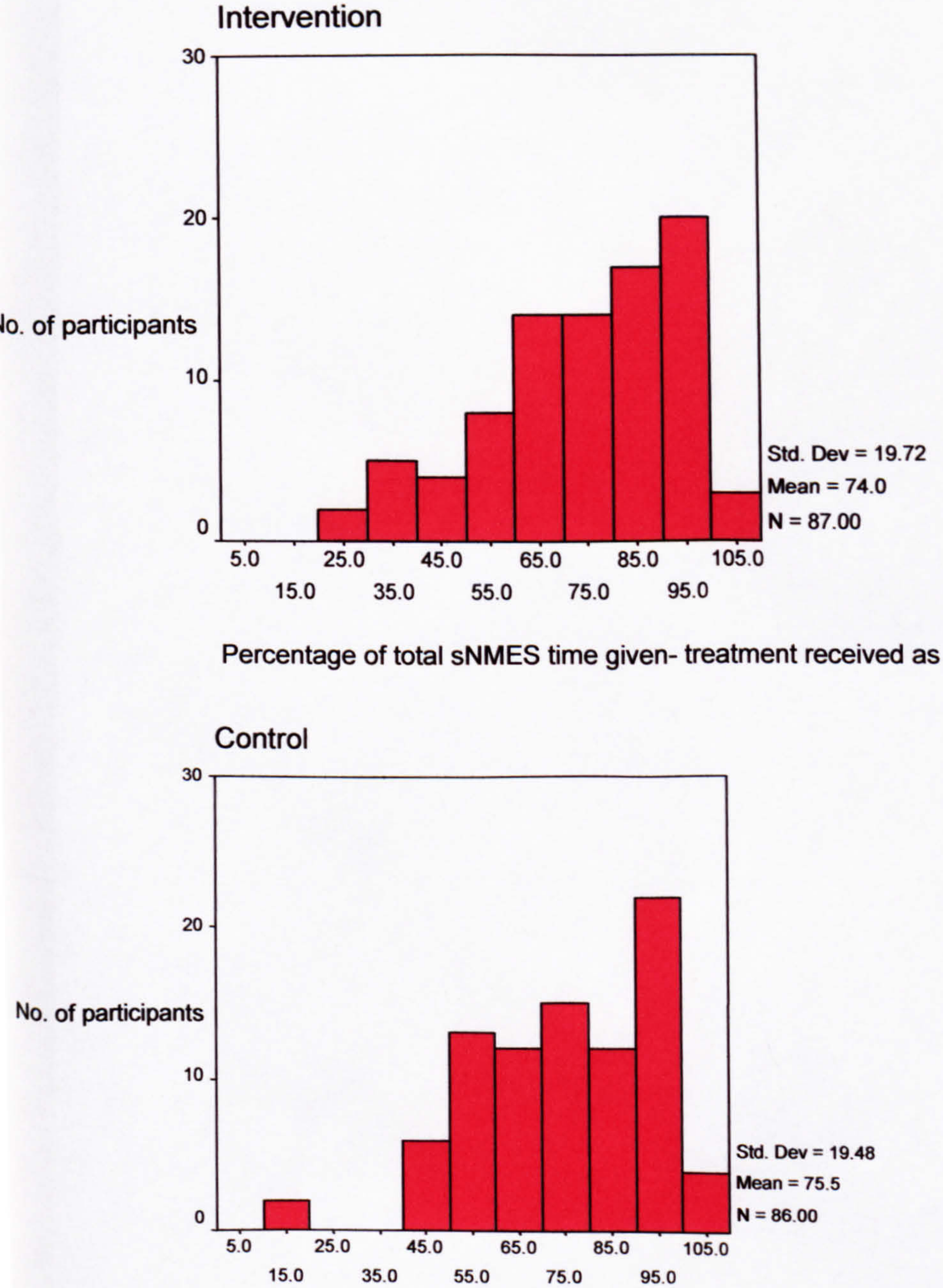


Table 42: Percentage of total sNMES received as prescribed

	Intervention (n=87)	Control (n=86)	All (n=173)
Mean	74.03	75.53	74.78
Standard deviation	19.72	19.48	19.56
Minimum	23.08	10.00	10.00
Maximum	100.22	102.79	102.79
Median [IQR]	77.3 [60.64-91.27]	78 [61.84-93.32]	77.7 [60.65-92.11]

It is of note that both the above analyses may be underestimates of the actual amount of stimulation received in view of the fact that we had to record sessions as 'missed' where only one of the start or stop times was documented.

(a) Treatment stopped early

The sNMES treatment was discontinued early in thirty eight participants for a variety of reasons (Table 43).

Table 43: Reasons for early discontinuation of sNMES course

Reasons for early discontinuation of sNMES course	Number of participants		
	All	Intervention	Control
Participant died	2	0	2
Participant withdrawn from study	2	1	1
Discharged home – passed ARAT*	7	4	3
Discharged home – participant unable/unwilling to continue sNMES at home	7	3	4
Discharged home – no reason given by nursing staff for discontinuing the sNMES on discharge	4	0	4
Stimulation stopped by study staff due to subject non-compliance e.g. not tolerating treatment, subject unwell	6	4	2
Stimulation stopped at participant's request	5	3	2
Other (2 due to inter-hospital transfer, 1 due to side effects, 1 due to broken stimulator, 2 no reason given).	6	3	3

* Participants planned for discharge during the sNMES course performed the ARAT[6, 7] and were discharged without the sNMES if they achieved the maximum score. This was only undertaken for the first 6 months of the study as it was found to be impractical.

(b) Treatment sessions missed

The maximum potential number of sessions given to each participant was 82. For the 173 diaries available, this is a total of 14186 sessions. As described above, some of the treatment courses were stopped early, accounting for 1644 missed sessions. Out of the remaining 12542 sessions, 2930 (23%) were not given. The reasons for these 2930 missed treatment sessions are shown in Table 44.

Table 44: Reasons for missed sNMES sessions

Reason sNMES session not given	Intervention	Control	All
Not stated (e.g. no start/stop time, box left blank, 'not given' box ticked but no reason given	1152 (75%)	1127 (81%)	2279 (78%)
Technical (e.g. no stickers, battery problems etc.)	92 (6%)	56 (4%)	148 (5%)
Unavailable for treatment (e.g. off ward/out of house)	86 (6%)	62 (4%)	148 (5%)
Participant reasons	120 (8%)	55 (4%)	175 (6%)
	n (% of participant reasons)	n (% of participant reasons)	n (% of participant reasons)
Painful	10 (8%)	0	10 (6%)
Anxious	3 (3%)	0	3 (2%)
Unwell	8 (7%)	2 (4%)	10 (6%)
Tired	1 (1%)	0	1 (1%)
Asleep	4 (3%)	9 (16%)	13 (7%)
No reason	58 (48%)	39 (71%)	97 (55%)
Non-compliant	30 (25%)	4 (7%)	34 (19%)
Other	6 (5%)	1 (2%)	7 (4%)
Staff reasons – forgot, subject unwell, busy, other	55 (4%)	62 (4%)	117 (4%)
Other e.g. blisters, rash	21 (1%)	9 (1%)	30 (1%)
Discharged home - without stimulator, or passed ARAT	17 (1%)	16 (1%)	33 (1%)
Total	1543 (100%)	1387 (100%)	2930 (100%)

6.2 Summary

- The amount of sNMES actually received by participants was similar between randomisation groups.
- Participants received 67.8% of intended stimulation and this was similar between groups.
- The sNMES course was discontinued early in 38 participants. Four of the participants in the control group (compared with none in the intervention group) were discharged without their stimulator with no reason given. Other reasons for early discontinuation of the sNMES course occurred with similar frequency between groups.
- During the treatment courses, 23% of sessions were missed. No reason was given for the majority of these missed sessions. Participant reasons of pain, anxiety, and tiredness were only seen in the intervention group.

Chapter 7 Inter-observer study

7.1 Background

In this study, outcome measures chosen were valid, reliable, relevant and feasible to use. The initial assessments were all undertaken by the research fellow (CC), and the outcome assessments by 2 research nurses. This inter-observer study was undertaken to look at the inter-observer reliability of our outcome measures. We wanted to ensure that there was good reliability, i.e. minimal inter-observer variability, between the 2 nurses, and between the nurses and the research fellow (CC).

7.2 Methods

The most appropriate statistical approach to analyse the level of agreement between the two observers for continuous data is to use the methods described for assessing agreement between two methods or observers. The methods used involve graphical techniques and simple calculations to determine the relation between differences to the mean, and to estimate limits of agreement. It should be noted that the correlation, a measure of linear association, is often erroneously interpreted as a measure of agreement.

For the categorical measures (i.e. the Shoulder Shrug Test[71] and FAT[8]) the level of agreement can be determined by the kappa statistic[202]. The kappa statistic is becoming an increasingly common tool for determining agreement between two observers. It is also more appropriate than other methods such as calculating the correlation coefficient which is a measure of association rather than agreement. Kappa has a maximum value of 1.00 when agreement is perfect, and a value of 0 indicates no agreement better than chance. A weakness of the kappa statistic is that it takes no account of the degree of disagreement, therefore the weighted kappa can be calculated which gives different weights to the disagreements according to the magnitude of the discrepancy.

Inter-observer agreement was measured for both the primary outcome measure (the ARAT[6, 7]) and the objective secondary outcome measures (the Motricity Index[9], FAT[8], Shoulder Shrug Test[71], passive and active range of pain free movement[130, 131] and upper arm girth). As these measures are included in both the 4 week and 3 month assessments, the inter-observer assessment was completed for either assessment. A short questionnaire

(Appendix 2.18) for the inter-observer comparisons was compiled from the relevant sections of the main assessment proformas.

The inter-observer agreement was measured on two separate occasions, the first set (A) of comparisons were between the two research nurses and the second (B) between one of the research nurses and the research fellow (CC). Patients due their 3-month or 4 week assessment were contacted by one of the research nurses, either in person if they were still in hospital, or by telephone if they had been discharged.

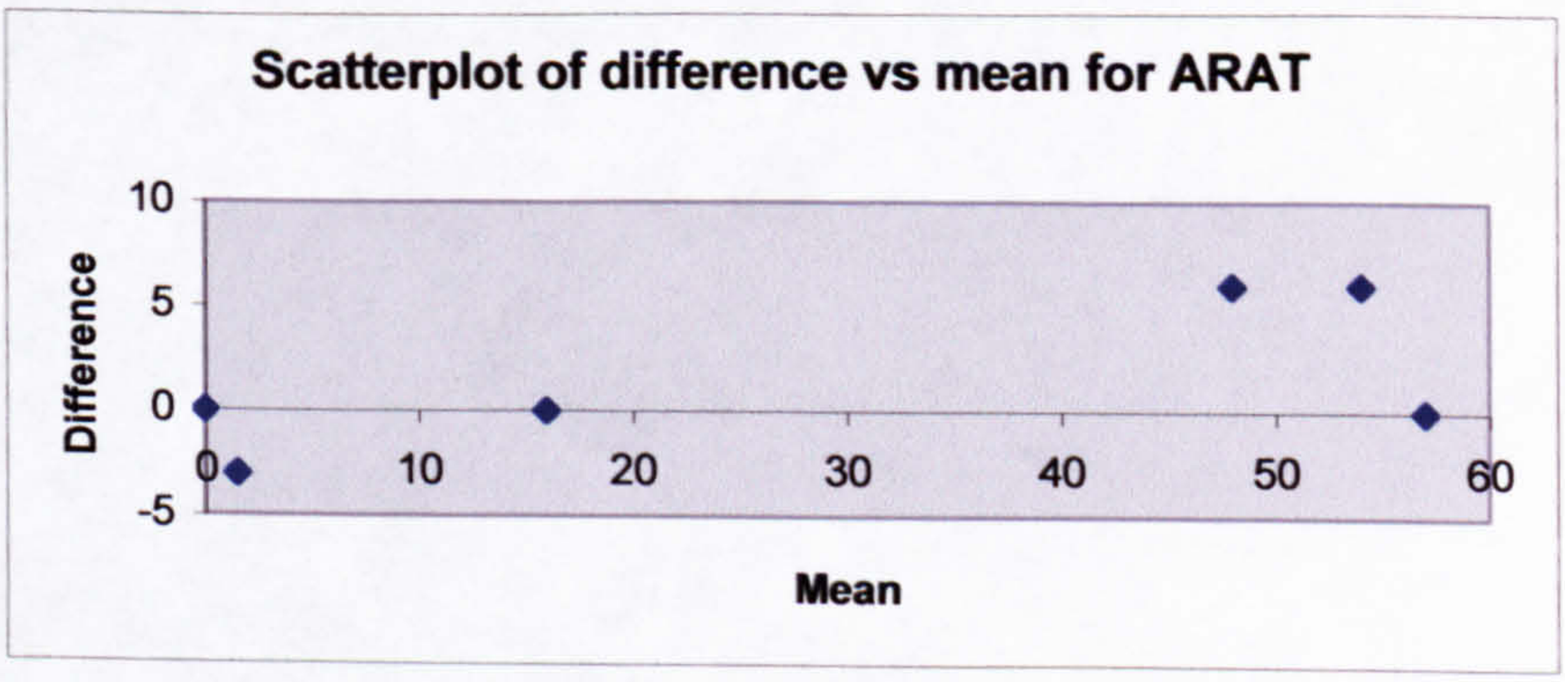
On both occasions that the inter-observer agreement was measured, half of the patients received their study assessment first and half received the inter-observer agreement assessment first to remove any potential bias for the second series of assessments.

7.3 Results

A total of 16 patients were recruited, eight on each of the two occasions that the inter-observer variability comparisons were made.

The scatterplot (Figure 10) shows the difference in the ARAT[6] scores vs. the mean ARAT[6, 7] score for inter-observer test B. From the scatterplot the relationship between the measurement and true value can be seen. As we do not actually know the true value, the mean of the two measurements is the best estimate that we have. We can see visually that the differences do not appear to be related to the magnitude of the ARAT measurement.

Figure 10



The scatterplots for the other continuous variables for inter-observer test B are shown in Figures 11 to 14. The relationships between the measurement and true value can be seen and, as with the ARAT, the differences do not appear to be related to the magnitude of the measurement.

Figure 11

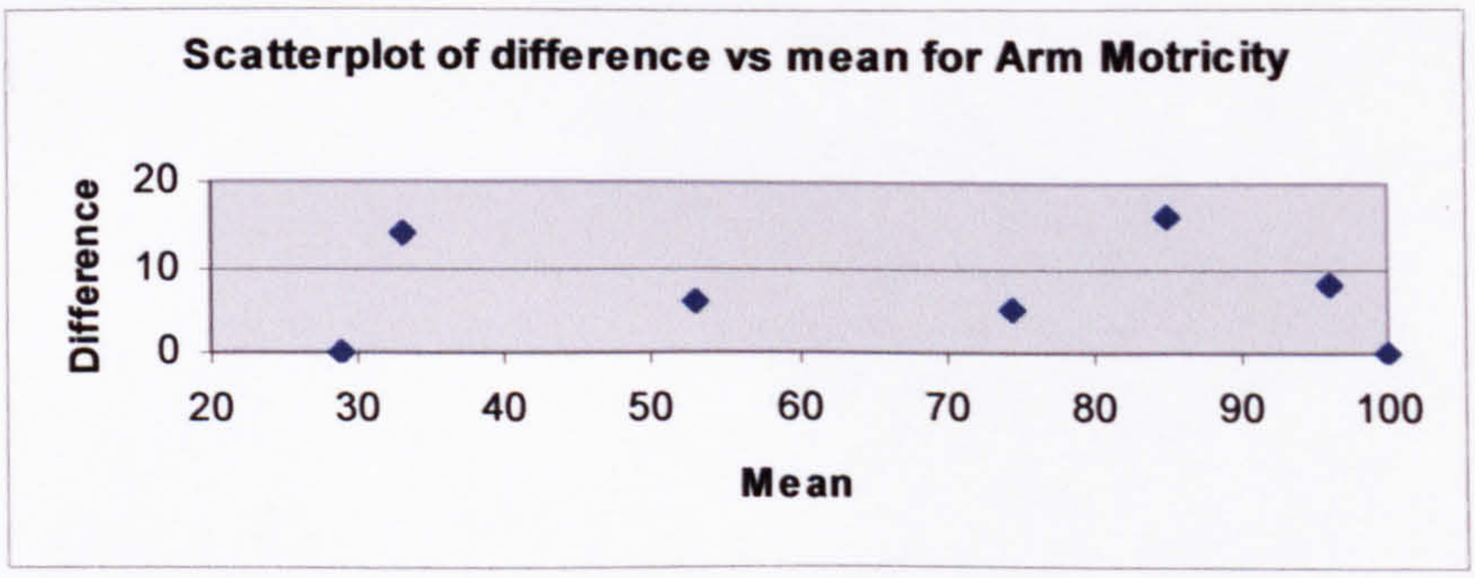


Figure 12

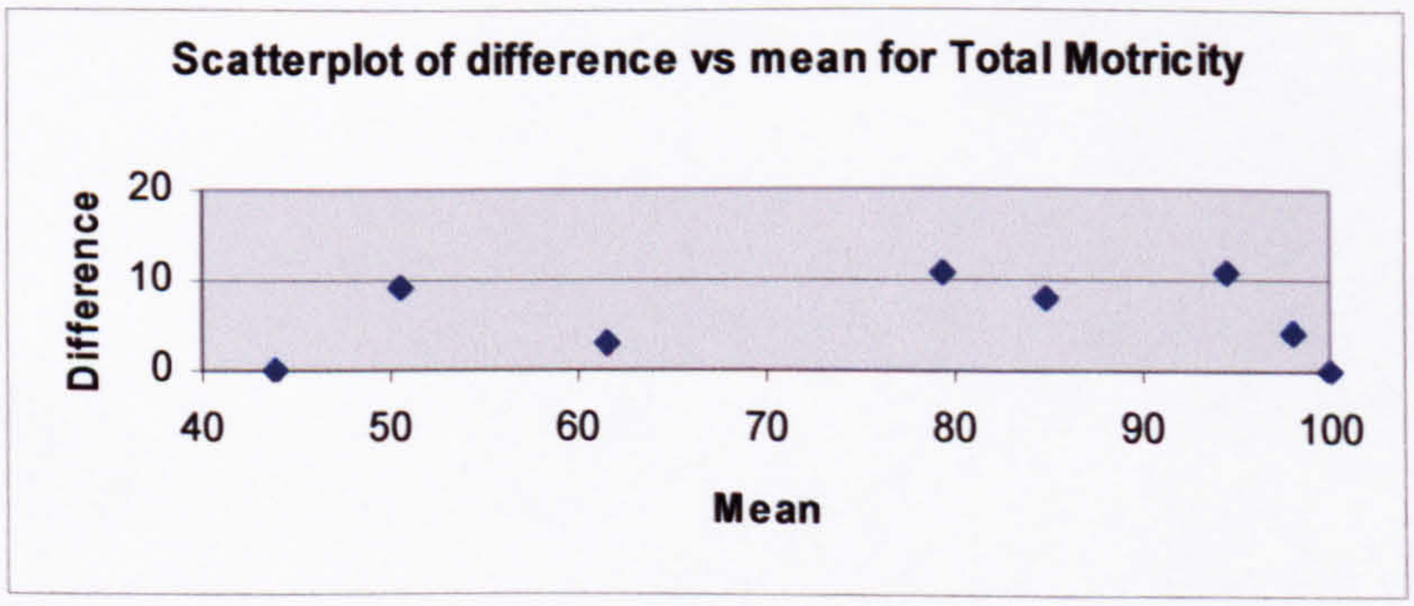


Figure 13

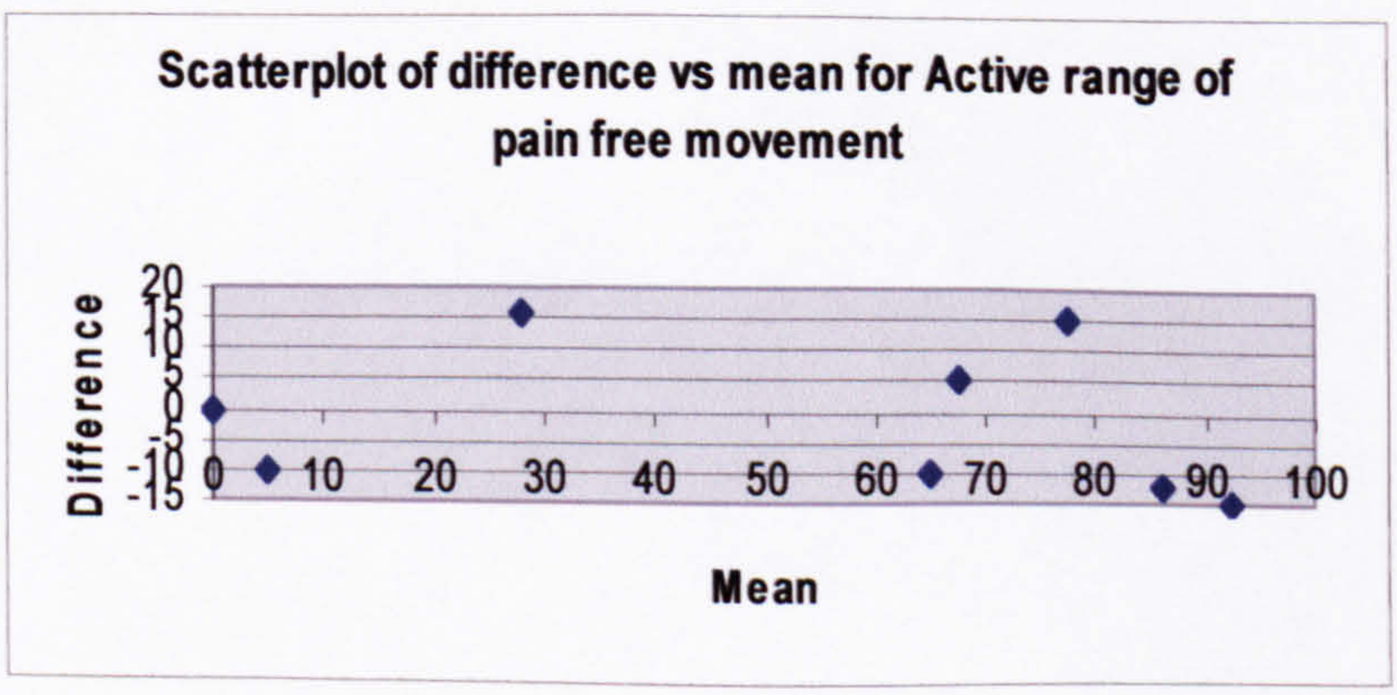
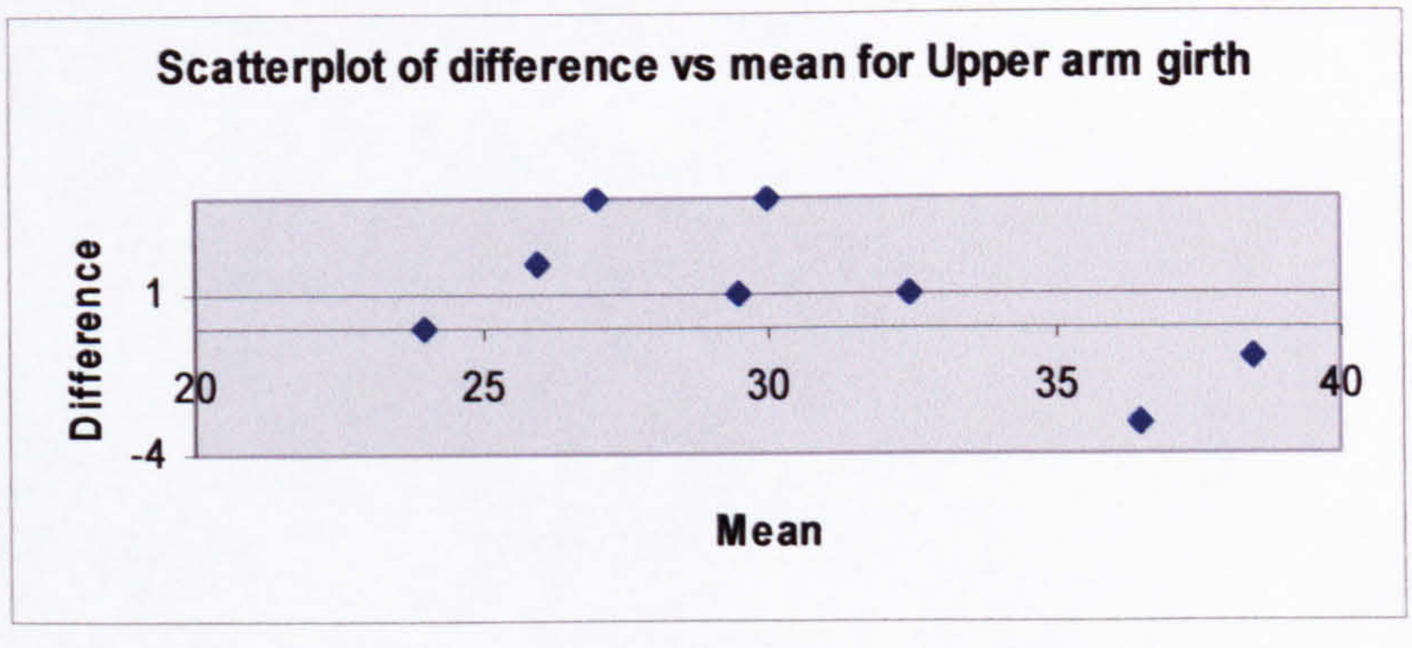


Figure 14



The ARAT[6] scores for both Observer 1 and Observer 2, the mean of the two scores and the difference for inter-observer test B are seen in Table 45.

Table 45

ARAT Observer1	ARAT Observer2	Mean Score	Difference between the scores
57	57	57	0
57	51	54	6
0	3	1.5	-3
0	0	0	0
16	16	16	0
57	57	57	0
51	45	48	6
57	57	57	0

Table 46 shows the 95% limits of agreement for the continuous measures. All measures lie within the 95% limits of agreement, except the difference for the Total Motricity Index score[9] in test A.

Table 46

Outcome measure (for affected side)	Inter-observer test –A (research nurse vs. research nurse) 95% limits of agreement	2nd Inter-observer test –B (research nurse vs. research fellow) 95% limits of agreement
ARAT[6]	-12 to 13	-5 to 7
Arm Motricity Index score[9]	-20 to 36	-6 to 19
Total Motricity Index score[9]	-13 to 19†	-3 to 15
Active range of pain free movement[130, 131]	-17 to 84	-26 to 23
Upper arm girth	-9 to 5	-4 to 6

† Max difference 20.5 outside the 95% limits of agreement

Table 47 shows the weighted kappa statistics for the categorical measures.

Table 47

Outcome measure (for affected side)	Inter-observer test –A (Research nurse vs. Research nurse) Weighted Kappa	2nd Inter-observer test –B (Research nurse vs. Research doctor) Weighted Kappa
Shoulder Shrug Test[71]	0.69*	0.69*
Frenchay Arm Test[8]	0.83**	0.90**

0.41-0.60 Moderate agreement
* 0.61-0.8 Good agreement
** 0.81-1 Very good agreement

7.4 Summary

These analyses of inter-observer agreement include only a very small number of participants due to both practical and time constraints. The results must therefore be interpreted with caution. The 95% limits of agreement are fairly wide, reflecting the very small sample sizes. The mean difference, shown in the scatterplot (Figure 10) is an estimate of the average bias of one observer against the other. So the closer the points are to zero, the better the agreement. One also needs to consider how well the observers agree for an individual patient, which can be done by using the standard deviation to construct the 95% limits of agreement.

There are difficulties with the use and interpretation of the kappa statistic, particularly as it depends on the proportion of subjects in each category, because the expected frequencies, by chance, can be very different, depending on the specific data distribution. The weighted kappa values for the first test of agreement (A) showed good agreement for the Shoulder Shrug Test[71] and very good agreement for the FAT[8] between the two research nurses. The second test (B) showed good agreement for the Shoulder Shrug Test[71] and very good agreement for the FAT[8] between the research nurse and research fellow (CC).

Good agreement between the observers is only likely if the methods used are both accurate and repeatable. Whilst we did not have the resources to make any assessment of repeatability of any of the assessments for the same observer with the same patients, these measures have been widely validated in other studies.

Chapter 8 Discussion

This randomised controlled trial was undertaken to evaluate a 4-week programme of surface neuromuscular electrical stimulation (sNMES) for patients with upper limb impairment following acute stroke. The results showed no statistically significant difference in arm function between groups in terms of the primary outcome measure, the total ARAT[6, 7] score at 3 months after stroke.

There were significant differences in favour of the control group when using other measures of arm function (subsections of the ARAT[6, 7]; FAT[8]), and upper limb impairment (the Arm subsection of the Motricity Index[9]) at 3 months. Despite these differences in secondary outcomes, this did not influence disability (ADLs) at 3 months. No significant differences in upper limb pain, visuospatial impairment or global health status were seen between groups at 3 months. There were no statistically significant differences between groups in any of the outcome measures at 4 weeks.

The primary results of the study were neutral i.e. a 4 week programme of sNMES to the shoulder did not improve upper limb function when initiated within 10 days of stroke onset. However, a number of secondary outcomes (upper limb impairment, other measures of arm function) were better in the control group 3 months after stroke. This was an unexpected result. These differences were not seen at 4 weeks i.e. immediately after the intervention period. None of the previous studies of sNMES to the upper limb after stroke have reported unfavourable outcomes in the intervention group.

The following need to be considered in order to try to understand and explain these results:

- study design: strengths and weaknesses
- sNMES regime and delivery
- mechanism by which sNMES can affect upper limb recovery

8.1 Study design: strengths and weaknesses

The study design and conduct was robust and did not have some of the weaknesses of previous studies.

8.1.1 Setting

Study participants were typical stroke patients who were treated by two specialist stroke services within the same NHS Trust. The majority of previous studies did not state the setting where the research took place. A specialist service is the ideal setting for randomised controlled trials of stroke rehabilitation as this is currently the 'gold standard' for stroke care.

8.1.2 Eligibility

Subjects with a wide range of upper limb impairment were recruited. All participants were required to have evidence of upper limb weakness/drift and/or finger-nose in-coordination and/or visual inattention. However, nearly all had some degree of weakness and none had visual inattention alone. There is a wide variation in beliefs as to who this intervention is appropriate for and, in clinical practice, it is given to patients with both mild and severe deficits. We believe that our patients are similar to those in previous studies of ES to the upper limb following stroke. Subjects recruited for studies of EMG-stim and PFST were required to have some movement of the upper limb at baseline[143, 158], but most other previous studies did not recruit patients based on their initial level of upper limb weakness or impairment (Table 3)

Although eligibility criteria were broad and clearly defined, only 12% of stroke admissions were recruited (Figure 4). The inclusion criteria were appropriate as most subjects for whom the intervention was clinically indicated were included; 28% were excluded because they had no upper limb deficit, 10% received palliative care and 12% had previous significant co-morbidity which would have affected treatment or assessments (Table 5). By widening the time window and geographical area for recruitment, it would have been possible to have increased participation. However, the study was designed to look at the effect of early treatment, and it was not logistically possible to cover the whole of Northumberland.

Some of the previous studies of ES have not reported exclusion criteria or the population screened[155, 167]. Other studies have detailed exclusions but with some important omissions. For example, Faghri et al[82] excluded subjects if they had a permanent pacemaker in situ, but did not report excluding any other subjects e.g. those with previous shoulder problems.

8.1.3 Initial assessment

This was undertaken by a single observer (CC) using a standardised protocol. Where possible, validated instruments were used, and when these were not available data items were clearly defined. The initial assessment was comprehensive, covering demography, pre stroke characteristics and neurological deficit. Intervention and control groups were well matched at baseline. It is unlikely that an important baseline variable was omitted which could have produced an initial difference between intervention and control groups, accounting for the differences in secondary outcomes at 3 months.

Some previous studies have reported little or no demographic data or clinical features of study subjects[143, 173]. Others have reported baseline demographics but do not appear to have made other important initial assessments e.g. pain[82].

8.1.4 Randomisation

This was by a central independent computerised randomisation service. Less than 50% (8/17) of previous studies had a secure randomisation process.

8.1.5 Treatment received by intervention and control groups

Within a RCT, the treatment received by randomisation groups should differ only in receipt of the intervention. The amount of sNMES or sham given was recorded, and randomisation groups did not differ in terms of this. Compliance with treatment was similar for both groups. Very few sessions were missed because of reported side effects (10/1543 sessions, all of which were in the intervention group) (Table 44). There was no formal reporting system for adverse events so this may be an underestimate. The study relied upon participants and staff to complete diaries and there were a number of occasions when the reason for missed sessions was not recorded. The sNMES course was well tolerated and was discontinued early in only 5 cases (3 intervention, 2 control) at the participants' request.

The amount of upper limb rehabilitation received during the intervention period was not measured, but similar numbers in each randomisation group were still receiving physiotherapy at 3 months (Table 12). It is possible but unlikely that randomisation groups received different amounts of therapy during the ES treatment period. Differences in the intensity of general and upper limb physiotherapy and occupational therapy could account for the results. A recent systematic review has shown that early intensive stroke rehabilitation may be associated with enhanced recovery after stroke[45]. If the intervention

group did receive less therapy this could have been because they were less inclined to participate because of tiredness, pain or other adverse effects which were not reported or recorded. Fourteen participants (18%) in the intervention group attributed shoulder pain to the stimulator.

Another explanation for possible differences between the amount of therapy received may have been that therapists were less likely to interrupt ES sessions for those with an active stimulator. Therapists and nurses were not informed of the subjects' randomisation groups but may have been aware of the treatment by their own observations. There may have been other differences between groups in the treatment provided by stroke unit staff or ways in which patients and carers spent their day which were not measured or considered.

Only two previous studies of ES have looked at compliance with treatment[152, 167]. Both reported very high compliance levels. None have reported the amount of physiotherapy and occupational therapy received.

8.1.6 Blinding

Subjects

Participants were not informed of randomisation group allocation, and a sham stimulator was given to control subjects. The active stimulator did produce a regular visible movement of the shoulder so complete blinding was not possible. However, not all subjects could identify whether or not they had received active treatment. At 3 months, 71% of the intervention group thought that they had had active treatment compared with 20% of subjects in the control group (Table 16). In previous studies of ES to the upper limb, very few (5/17) have used sham treatments.

Stroke unit staff

The treatment regime and placement of electrodes was undertaken by a single researcher (CC) who prescribed treatment, specifying the stimulator settings. Other than connecting the stimulators, nurses were not involved in adjusting the ES. Physiotherapists were not involved in delivery of the ES. Staff were not informed of the subjects' randomisation groups but may have been aware of the treatment by their own observations. The opinions of staff as to whether subjects were receiving active or sham treatment were not sought. Neither were their views about the efficacy of ES. Previous studies have not discussed the blinding of clinical staff.

Outcome assessors

Outcome assessments were undertaken by two research nurses who were blinded to the participants' randomisation groups. We believe that this blinding was secure. However, the nurses were not asked to guess the group allocation at any stage or to indicate whether or not the participant had given an opinion regarding their randomisation group prior to the final question of the 3 month assessment. We did not ask the outcome assessors to give their views regarding group allocation as we felt that this would have introduced bias. The assessors questioned the participants regarding their views at the end of the 3-month assessment so that they weren't unblinded during outcome assessments. Outcomes were undertaken by blinded assessors in 11/17 previous studies.

8.1.7 Drop outs and data completeness

Losses to follow up and missing data were not a problem in this study (Figure 4). Eighteen participants died (9 in each group). Only one participant was lost to follow up and two refused. The level of follow-up in previous studies was similar.

8.1.8 Analysis

Analysis was on an intention to treat basis. This method was also used in the majority of previous studies.

8.1.9 Outcome Assessments

Stroke patients wish to regain useful upper limb movement, so the primary outcome measure chosen for this study was upper limb function. Previous studies have looked at the effect of ES on subluxation, motor recovery and pain, and although there is evidence of the beneficial effect of ES on these, it is not clear whether this translates into improved functional recovery.

A range of scales of upper limb disability, pain and impairment were used. These were relevant to the intervention and have previously been widely used in trials of upper limb rehabilitation after stroke. Although there is evidence that ES is beneficial in improving joint alignment (i.e. reducing or preventing subluxation) and reducing spasticity[5, 62], these outcomes were not measured in this study. There is often confusion when trying to define subluxation[33], and its measurement is unreliable and often of no new clinical significance[181]. There is no validated measure of upper limb spasticity other than at the elbow[156].

The timings of outcome assessments were chosen to coincide with the end of the treatment period and to look at longer term effects. These time points have also been used in previous studies. A longer period of follow up would have been desirable to see if the differences at 3 months were sustained. As analysis of outcomes was not undertaken until the final outcome measure was completed, it was not possible to undertake a 6 or 12 month assessment once the results of the study became available.

The primary outcome was arm function measured by the Action Research Arm Test (ARAT)[6, 7]. This is a robust test which measures 4 domains of upper limb function: grasp, grip, pinch and gross. Its limitation is that subjects have to be able to sit to perform the test. It also has a ceiling effect i.e. subjects achieving a maximal score may still have a degree of upper limb impairment. Although there were no significant differences in total ARAT[6, 7] score between intervention and control groups, differences were seen in the grasp and gross subsections at 3 months. These subsections involve predominantly proximal rather than distal movement (i.e. shoulder movement), and are those most likely to have been influenced by the intervention.

Upper limb outcomes were also worse in the control group at 3 months for the Arm Motricity Index[9] and Frenchay Arm Test (FAT)[8]. The fact that four of our secondary measures of upper limb outcome show significant differences between intervention and control groups makes it unlikely that this is a chance finding.

Electrical stimulation has been used to treat and prevent shoulder pain[5]. There was no difference between groups in the prevalence of shoulder pain. Pain was assessed using both a 5-point severity scale and a 0-10 numerical rating scale[127, 128]. The severity scale alone can be insensitive to small changes, but its sensitivity can be increased by using it together with a numerical rating scale. Pain was also assessed by measuring pain-free range of humeral lateral rotation[130, 131] which has been used successfully in a previous study of electrical stimulation[132]. A Visual Analogue Scale was not used to measure pain as previous work has shown that many stroke subjects are not able to complete these scales successfully[129].

At the 3-month assessment, participants were asked whether or not they had experienced symptoms from the ES, and to give their views on which stimulator they thought they had received. Ideally, more information should have been sought regarding their views, including the acceptability of ES and how the treatment affected their daily activity.

8.1.10 Study Size

This is the largest study to date of electrical stimulation to the upper limb following acute stroke. The study had adequate statistical power. Surprisingly, a 'clinically significant difference' in ARAT[6, 7] scores has not previously been defined and a pragmatic decision to define it as a difference of 8 points was made. No similar definition has been made in previous studies[1, 52, 59, 152].

8.1.11 Conflict of interest

There was no conflict of interest for any member of the study team.

8.2 sNMES regime and delivery

In this study, ES to the shoulder did not improve outcome following acute stroke and may have had a detrimental effect on upper limb recovery. This could have related to the sNMES regime and/or delivery.

8.2.1 Site

The ES was applied to the shoulder as there is evidence that proximal upper limb recovery precedes distal recovery[66]. Electrical stimulation to the shoulder is widely used in clinical practice and is thought to be a safe method of improving upper limb outcome following stroke[5, 62]. The ES may have had a detrimental effect on proximal recovery i.e. at the shoulder (suggested by the differences in the grasp and gross subsections of the ARAT[6, 7] at 3 months). Studies of ES to the distal upper limb have reported motor improvements with the treatment[88, 154, 158]. Whilst it is unclear whether these improvements translate into functional benefit, there has been no suggestion that ES to the distal upper limb has a detrimental effect on either motor or functional recovery[88, 154, 158].

8.2.2 Duration, frequency and intensity

The ES regime chosen was one that has been used in previous studies and is widely accepted in clinical practice. No evidence exists regarding the optimal regime in terms of duration and frequency.

The intensity of ES given to subjects in the intervention group was at a level required to produce a comfortable gross movement of the shoulder. Again, this is accepted practice

and this method has been used in previous studies of ES to the shoulder. The optimal intensity of ES is not known.

It is conceivable that subjects in the intervention group were given suboptimal ES in terms of duration, frequency and/or intensity. This might explain why no beneficial effects were seen in the intervention group, but does not account for the fact that those in the control group achieved higher scores in some of the secondary outcome measures at 3 months.

8.2.3 Supervision of ES treatment

No therapists were involved in the delivery of the ES, and it is possible that the intervention stimulators were applied wrongly and thus had a detrimental effect on upper limb recovery. However, the ES machines were checked regularly by the research fellow (CC), and electrode sites marked to ensure correct positioning. Also, if the ES was applied incorrectly, those in the intervention group may have reported more pain at 4 weeks than those in the control group, and this was not the case (Table 11).

8.2.4 Effect on other treatment

As already discussed in Section 8.15, those in the intervention group may have received less therapy.

8.2.5 Study participants

Participants in the study were typical stroke patients. There is no reason to suggest that the ES would have affected these patients any differently from stroke subjects in previous ES studies, or stroke patients in clinical practice.

8.2.6 Timing of the ES

Most functional recovery occurs within the first 6 months after stroke and is most rapid within the first few weeks [64]. It is thought that early intervention offers the greatest opportunity to improve recovery[45, 46]. A review of ES by Ada et al in 2002[184] concluded that early, rather than late, ES may enhance upper limb motor recovery following stroke. Subjects were, therefore, recruited early after stroke in this study, although the ideal time is not known. It was a pragmatic decision to recruit within the first 10 days following acute stroke. Many previous studies of electrical stimulation have recruited patients several months or years after stroke.

8.3 Mechanisms by which sNMES can affect upper limb recovery

Surface neuromuscular electrical stimulation has been proposed as a safe method of improving upper limb outcome following stroke by a variety of mechanisms. It is thought to promote motor re-learning through afferent stimulation to the somatosensory cortex, and through effects such as muscle strengthening, enhanced joint alignment and reduction in spasticity and pain[5, 62].

In this study, however, the sNMES may have had a detrimental effect on upper limb recovery. No differences were seen between groups at 4 weeks, so the effect was seen after the sNMES had been discontinued. The sNMES may have interfered with motor re-learning processes, influencing and impeding recovery after the treatment period.

Previous experimental models have suggested that very early constraint therapy and early overuse after cerebral ischaemia in rodents may be harmful[203, 204]. The relevance of this is not known in humans but these are possible explanations for the differences seen between groups at 3 months in this study. As the intervention stimulator produced movement of the shoulder, it is possible that whilst it was being given participants used their affected arm less i.e. the stimulator promoted learned non-use of this arm. Alternatively, the movement produced at the shoulder may have resulted in early over-use and thus adversely affected upper limb recovery.

Previous studies of ES in patients with cerebral palsy, head injury and spinal injury have not reported a detrimental effect on recovery[170, 205, 206].

8.4 Subgroup and secondary analyses

There was one pre-planned subgroup analysis in this study. This was to look at the outcomes of participants with mild/moderate upper limb function (ARAT>0) and those with severe functional impairment (ARAT=0) at the initial assessment. We chose to look at initial ARAT[6, 7] score as there is evidence that the severity of initial upper limb motor impairment is a predictor of upper limb recovery[3, 65]. There is also some evidence that ES is more beneficial in stroke patients with a milder degree of upper limb impairment[155] .

There was no difference in any of the outcome measures at 4 weeks or 3 months between intervention and control groups for those with mild/moderate upper limb impairment. Those

with severe functional impairment in the control group had significantly better outcomes – grasp and gross subsections of the ARAT[6, 7] and Arm Motricity Index[9]. No difference was seen at 4 weeks.

The negative effect of sNMES to the upper limb following acute stroke was seen only in those with initial severe impairment. The potential reasons for this observation are discussed in Section 8.3 and include an adverse effect of sNMES upon natural recovery, over-stimulation of the affected arm, and learned non-use. Hypotheses to explain why the negative effect was only seen in those with severe impairment include:

- Surface NMES impedes recovery by producing abnormal afferent stimulation and inhibiting plasticity in a group who are not receiving any other afferent stimulation to the upper limb.
- Those with severe impairment may have been less aware of the stimulation and therefore less likely to report adverse events or be aware if the stimulator was wrongly delivered.
- Over-stimulation may have produced tiredness and shoulder subluxation in this group. Neither of these effects was measured.
- Those with severe initial impairment may also be more likely to develop learned non-use.

Further analysis was undertaken once these results were available. However, the results from further subgroup and secondary analyses should be regarded as hypothesis-generating as they were not pre-specified.

As the results of our single pre-planned subgroup analysis showed that the negative effect of sNMES was only seen in those with initially severe upper limb impairment, we chose other subgroups which were measures of stroke severity: the presence or absence of shoulder weakness at baseline (measured by the Shoulder Shrug Test[71]), the NIHSS[197], and the stroke subtype (TACS/PACS vs. LACS/POCS)[198].

The ES had a detrimental effect on recovery in those with moderate to severe shoulder weakness at baseline, which is consistent with our findings in the ARAT=0 group. However, it also appeared to have had a negative effect on recovery in those with less severe strokes and in those with LACS or POCS. These negative effects in the less severe and non-cortical strokes could have been due to overuse or learned non-use but it seems unlikely that they relate to a direct influence on cortical plasticity. The results must, however, be interpreted

with caution. It is noteworthy that differences were also seen in favour of the control group in those with more severe strokes and in those with TACS/PACS, but they did not reach statistical significance, possibly due to the small numbers in these groups. There may also have been a ceiling effect in less severely impaired subjects.

In the subgroup analysis according to side of impairment, the detrimental effects of ES on recovery were seen in those with left sided impairment. We hypothesised that this might have been because these were right hemisphere strokes and so more likely to have visuospatial and sensory deficits. The absence of afferent input in these cases may have meant that these subjects were more susceptible to the negative effects of ES on natural recovery, and the possible effects of over-stimulation and learned non-use. However, the subgroup analyses showed that those without visuospatial and sensory deficits experienced negative effects from the ES. Again, these results must be viewed cautiously as differences were also seen between groups in those with visuospatial deficit and sensory loss but may not have reached statistical significance due to the small numbers in each group.

We also hypothesised that the differences seen between groups in subjects with left sided impairment may in fact be due to hand dominance. Our subgroup analysis showed that the negative effects of ES were seen in those with the non-dominant hand affected. These subjects may have been more susceptible to learned non-use from the ES. They may have been less likely to use their affected arm, if it was their non-dominant side, when the ES was in situ or in between sessions if the arm was tired. This may have been especially the case if their initial arm weakness was severe.

8.5 Implications for practice and future research

8.5.1 Implications for practice

It has been proposed that sNMES to the upper limb is a safe method of improving outcome after stroke but our results suggest that this assumption should be challenged. Surface NMES may, in fact, be harmful to certain stroke subjects and its use in routine practice cannot be recommended.

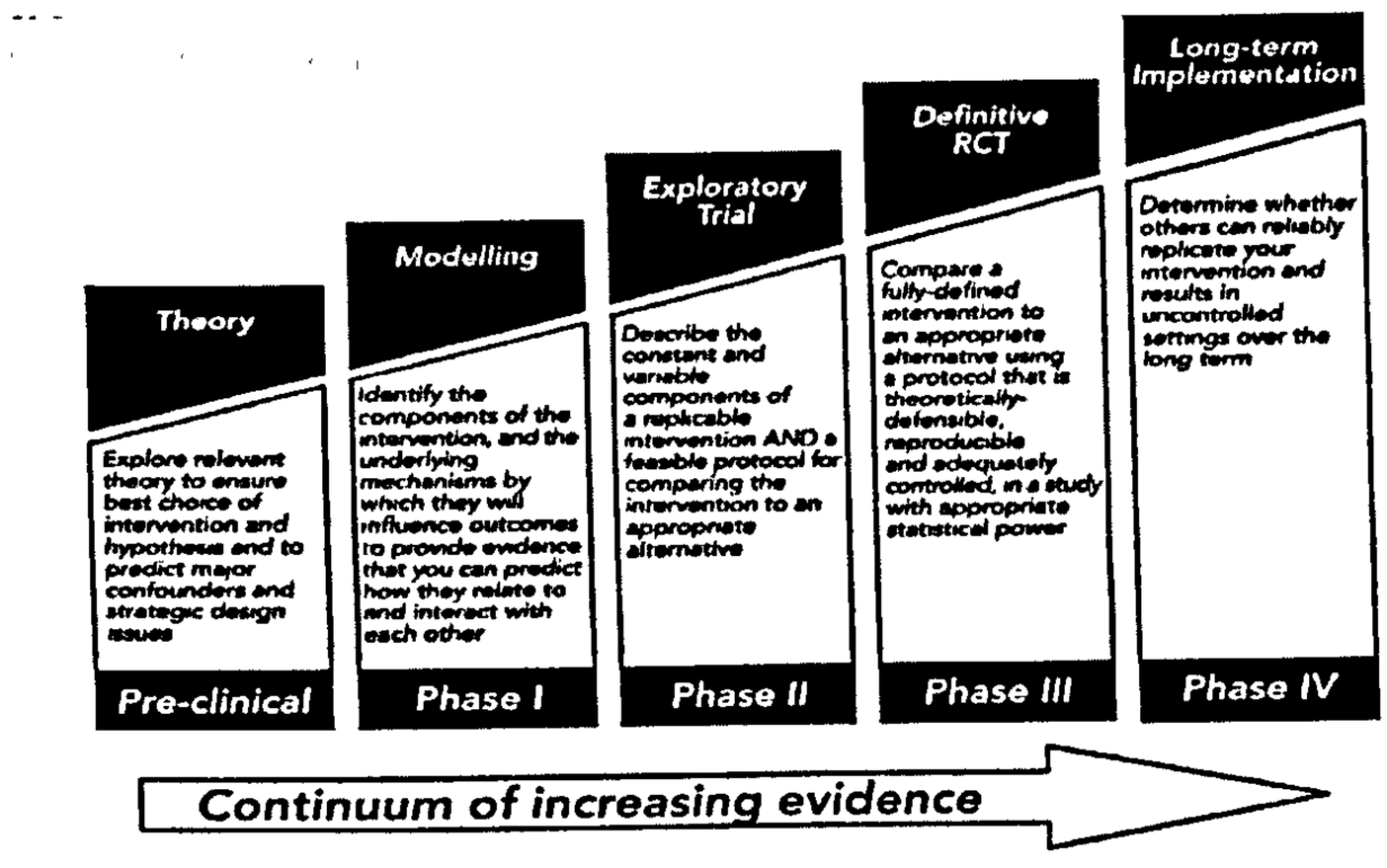
Those involved in the application of ES should be aware of its potential negative consequences, and of the lack of evidence to support its use in routine clinical practice. There is the potential for ES to be wrongly applied, and it should therefore only be given

under the supervision of specialists in the field. The costs of the ES equipment, therapist and nursing time, influence on other therapy input, and the inconvenience and possible discomfort to the patient must be weighed up against any benefits of ES treatment.

8.5.2 Future Research

We have scrutinised our results and the potential reasons for them, particularly since the ES may have had a detrimental effect on recovery in certain subjects. The Medical Research Council (MRC) framework[207] was available when we designed our study and at that time we felt that there was sufficient evidence to justify undertaking a definitive RCT. We have returned to this framework to address issues regarding further research in this area (Figure 15).

Figure 15: A framework for development and evaluation of RCTs for complex interventions to improve health (MRC)



8.5.2.1 Theoretical phase

In evaluating a complex intervention, the first step is to establish the theoretical basis that suggests that the intervention should have the effect(s) that it is expected to. Basic science and clinical studies have been undertaken to look at possible mechanisms of action of ES in upper limb recovery. A number of theories have been suggested: muscle strengthening, improved joint alignment; analgesic effects; improvement of visuospatial awareness. Studies have not addressed the mechanisms of action of ES with respect to theories of neurological recovery, particularly neuroplasticity and motor relearning. Electrical stimulation is widely used in clinical practice and we therefore felt comfortable proceeding with an RCT even though the mechanism of action was not clearly understood.

In retrospect, a clearer understanding about the effect of ES upon recovery following stroke is vital, and further research in this area should address this e.g. by the use of fMRI and PET.

8.5.2.2 Modelling phase

The next step is to develop an understanding of the intervention and its possible effects. It is vital to know the specific effects of an intervention on specific outcomes and measure these appropriately. ES is thought to improve the following upper limb outcomes: shoulder subluxation; upper limb pain; arm function; motor impairment. We felt that arm function was the most important clinical outcome. We did not measure subluxation as this is difficult to do reliably and is of doubtful clinical relevance. We recruited patients with a wide range of deficits because this was a pragmatic study, relevant to current clinical practice. Previous studies had suggested that certain subjects might gain more benefit from ES treatment e.g. those with less severe upper limb impairment at baseline[155], but none had suggested that ES could be detrimental to any subject groups. Reviews of the literature of ES to the upper limb following stroke have not re-analysed primary data, and a further meta-analysis of individual patient data may be warranted.

Future studies should recruit specific groups of patients, with clearly defined neurological deficits, who are most likely to benefit from ES treatment. Outcomes chosen must be relevant to the intervention effects studied, and also valid, reliable, sensitive and important to patients[208]. Patients' views should also be sought regarding their perceptions of ES and its acceptability.

8.5.2.3 Exploratory trial phase

Any intervention must be definable and reproducible and given by trained individuals. During this phase, testing of alternative forms ('doses') of an intervention can be undertaken. In drug studies, optimal dosages are developed but this is not done for interventions in rehabilitation studies. The optimal sNMES regime, in terms of duration and intensity, is not known. We reviewed the literature about regimes used in previous studies, and pragmatically chose one that had been used both in research and in clinical practice

The intervention must also be compared to an appropriate alternative and we used a placebo stimulator. We feel that further studies of ES must use a sham treatment for those in the control group. Ideally, a record of all other upper limb therapy should be kept[209, 210].

Although this can be difficult and time-consuming, it has previously been undertaken successfully by our research team[55]. We did not record routine therapy for this study because of the resources required to ensure that data collection was complete and accurate. In our previous single centre study, two research therapists were responsible for this task.

There should also be a formal mechanism in place for adverse event reporting in future trials.

The exploratory trial phase is also used to identify appropriate outcome measures and to make estimates of recruitment for a main trial. We based our methodology and power calculations on previous ES studies and on our previous studies of upper limb rehabilitation following stroke[55, 129].

8.5.2.4 Main trial phase

Our study was adequately powered and had robust methodology. Future studies should be similarly robust with adequate statistical power, be based in stroke units, and ideally be multi-centred to enable results to be generalisable. Outcome measures chosen in future studies should be relevant to the intervention studied, simple to use, and with proven validity and reliability in stroke patients.

8.5.2.5 Long-term surveillance phase

The final step in the evaluation of a complex intervention is a separate study to establish the long-term and real-life effectiveness of the intervention. Given that we have not demonstrated effectiveness a Phase IV study is not justified at present.

8.6 Conclusions

The primary results of the study were neutral i.e. a 4 week programme of sNMES to the shoulder did not improve upper limb function when initiated within 10 days of stroke onset. However, a number of secondary outcomes (upper limb impairment, other measures of arm function) were unexpectedly better in the control group 3 months after stroke, although this did not translate into differences in ADLs.

It is unlikely that the differences seen between the control and intervention group at 3 months were due to study design or conduct. Differences in upper limb therapy between

groups may explain these differences, as the amount of therapy received was not formally recorded. Potential pathophysiological mechanisms to explain these differences include an adverse effect of sNMES upon natural recovery, overstimulation of the affected arm, and learned non-use.

The use of ES to the upper limb following stroke cannot be recommended in routine practice. Further research in this area should address the effects of ES upon recovery following stroke. Studies should be adequately powered and have robust methodology. They should be undertaken in a stroke unit setting, and should study a specific intervention in a defined population using valid, reliable and relevant outcome measures.

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Appendix 1

1.1 Motricity Index

Arm (in sitting position)
A. Pinch grip; 2.5cm cube between thumb and forefinger
B. Elbow flexion; from 90 degrees, voluntary contraction/movement
C. Shoulder abduction; from against chest

A. Pinch grip

0	No movement
11	Beginnings of prehension (any movement of finger or thumb)
19	Grips cube, but unable to hold against gravity
22	Grips cube, held against gravity, but not against weak pull
26	Grips cube against pull, but weaker than other side
33	Normal pinch grip

Score R arm ☐☐ Score L arm ☐☐

B. Elbow flexion

0	No movement
9	Palpable contraction in muscle, but no movement
14	Movement seen, but not full range/not against gravity
19	Movement; full range against gravity, not against resistance
25	Movement against resistance, but weaker than other side
33	Normal power

Score R arm ☐☐ Score L arm ☐☐

C. Shoulder abduction

0	No movement
9	Palpable contraction in muscle, but no movement
14	Movement seen, but not full range/not against gravity
19	Movement; full range against gravity, not against resistance
25	Movement against resistance, but weaker than other side
33	Normal power

Score R arm ☐☐ Score L arm ☐☐

Leg (in sitting position)
D. Ankle dorsiflexion; from plantar flexed position
E. Knee extension; from 90 degrees, voluntary contraction/movement
F. Hip flexion; usually from 90 degrees

D. Ankle Dorsiflexion

0	No movement
9	Palpable contraction in muscle, but no movement
14	Movement seen, but not full range/not against gravity
19	Movement; full range against gravity, not against resistance
25	Movement against resistance, but weaker than other side
33	Normal power

Score R leg ☐☐ Score L leg ☐☐

E. Knee Extension

0	No movement
9	Palpable contraction in muscle, but no movement
14	Movement seen, but not full range/not against gravity
19	Movement; full range against gravity, not against resistance
25	Movement against resistance, but weaker than other side
33	Normal power

Score R leg ☐☐ Score L leg ☐☐

F. Hip Flexion

0	No movement
9	Palpable contraction in muscle, but no movement
14	Movement seen, but not full range/not against gravity
19	Movement; full range against gravity, not against resistance
25	Movement against resistance, but weaker than other side
33	Normal power

Score R leg ☐☐ Score L leg ☐☐

Arm score = scores (1) + (2) + (3) + 1 (to make 100) ***Leg scores (4) + (5) + (6) + 1 (to make 100)***

TOTAL RIGHT LEG ☐☐☐ **TOTAL LEFT LEG** ☐☐☐

TOTAL RIGHT ARM ☐☐☐ **TOTAL LEFT ARM** ☐☐☐

Side score = (ARM + LEG)/2

RIGHT SIDE ☐☐☐ **LEFT SIDE** ☐☐☐

1.2 Shoulder Shrug Test

- Subject should be sitting up straight.
- Ask subject to shrug both shoulders together.
- Observer watches for symmetry and then attempts to push down the shoulders.
- Normally it is not possible to force someone's shoulders down with moderate effort.
- Score each side in turn :

Scoring

0 = no shoulder elevation at all

1 = elevation of the shoulder, but less marked or weaker than the other side

2 = unable to force down the shoulder.

RIGHT SIDE ☐ **LEFT SIDE** ☐

1.3 Brunnstrom Fugl-Meyer Assessment

For arm movement			
Area	*Test*	*Scoring Criteria*	*Maximum Possible Score*
Shoulder/elbow/forearm	A. I. Biceps/triceps/finger-flexor reflexes	0 – no reflex activity 2 – reflex activity	4
	II. a. Flexor synergy Shoulder Elbow Forearm	0 – cannot be performed 1 – partial motion 2 – full motion	10
	b. Extensor synergy Shoulder Elbow Forearm	0 – no motion 1 – weak motion 2 – almost full strength compared to normal	8
	III. Volitional motion a. Hand to lumbar spine	0 – unable 1 – hand passes anterior superior iliac spine 2 – hand reaches lumbar spine	2
	b. Shoulder flexion 0-90 degrees	0 – unable 1 – partial 2 – able to perform 90 degrees shoulder flexion	2
	c. Forearm pronation-supination	0 – unable 1 - partial 2 – able	2
	IV. Volitional motion a. Shoulder abduction	0 – unable 1 - partial 2 – able	2
	b. Shoulder flexion 90-180 degrees	0 – unable 1 - partial 2 – able	2
	c. Elbow pronation-supination	0 – unable 1 - partial 2 – able	2
	V. Normal reflexes Biceps Triceps Finger-flexors	0 – two or three are markedly hyperactive 1 – one reflex is hyperactive, or two reflexes are lively 2 – no more than 1 reflex is lively	2
Wrist	B. Elbow 90 degrees, wrist stability Elbow 90 degrees, wrist flexion/extension Elbow 0 degrees, wrist stability Elbow 0 degrees, wrist flexion/extension Circumduction	0 – unable 1 - partial 2 – able	10

For arm movement			
Area	*Test*	*Scoring Criteria*	*Maximum Possible Score*
Hand	C. Fingers mass flexion Fingers mass extension Grasp a Grasp b Grasp c Grasp d Grasp e	0 – unable 1 - weak 2 – normal	14
	D. Coordination/speed Finger-nose test a. Tremor	0 – marked tremor 1 – slight tremor 2 – no tremor	2
	b. Dysmetria	0 – pronounced or unsystematic 1 – slight or systematic 2 – no dysmetria	2
	c. Speed	0 – six seconds slower than affected side 1 – two to five seconds slower 2 – less than 2 seconds Difference	2
Total upper extremity score for patient			66

For leg movement, sensation and balance			
Area	*Test*	*Scoring Criteria*	*Maximum Possible Score*
Lower extremity (supine)	E. I. Reflex activity – tested in supine position	0 – no reflex activity 2 – reflex activity	4
	II. a. Flexor synergy Hip flexion Knee flexion Ankle dorsiflexion	0 – cannot be performed 1 – partial motion 2 – full motion	6
	b. Extensor synergy (motion is resisted) Hip extension Hip adduction Knee extension Ankle plantar flexion	0 – no motion 1 – weak motion 2 – almost full strength compared to normal	8
Sitting (knees free of chair)	III. Movement combining synergies a. Knee flexion beyond 90 degrees	0 – no active motion 1 – from slightly extended position knee can be flexed but not beyond 90 degrees 2 – knee flexion beyond 90 degrees	2

For leg movement, sensation and balance			
Area	*Test*	*Scoring Criteria*	*Maximum Possible Score*
	b. Ankle dorsiflexion	0 – no active flexion 1 – incomplete active flexion 2 – normal dorsiflexion	2
Standing	IV. Moving out of synergy (hip at 0 degrees) a. Knee flexion	0 – knee cannot flex without hip flexion 1 – knee begins flexion without hip flexion but does not reach 90 degrees, or hip flexes during motion	2
	b. Ankle dorsiflexion	0 – no active motion 1 – partial motion 2 – full motion	2
Sitting	V. Normal reflexes Knee flexors Patellar Achilles	0 – two or three are markedly hyperactive 1 – one reflex is hyperactive, or two reflexes are lively 2 – no more than 1 reflex is lively	2
Supine	F. Coordination/speed – heel to opposite knee (5 repetitions in rapid succession) a. Tremor	0 – marked tremor 1 – slight tremor 2 – no tremor	2
	b. Dysmetria	0 – pronounced or unsystematic 1 – slight or systematic 2 – no dysmetria	2
	c. Speed	0 – six seconds slower than affected side 1 – two to five seconds slower 2 – less than 2 seconds difference	2
Total lower extremity score for patient			34
Balance	G. Sit without support Protective reaction non-affected side Protective reaction affected side Stand with support Stand without support Stand on non-affected leg Stand on affected leg	0 – unable 1 – partial 2 – normal	14

For leg movement, sensation and balance			
Area	*Test*	*Scoring Criteria*	*Maximum Possible Score*
Sensation – upper and lower extremities	H. i. Light touch a. Upper arm b. Palm of hand c. Thigh d. Sole of foot	0 – anaesthesia 1 – hyperaethesia/ dysaethesia 2 – normal	8
	ii. Proprioception a. Shoulder b. Elbow c. Wrist D. Thumb E. Hip F. Knee G. Ankle H. Toe	0 – no sensation 1 – three quarters of answers are correct, but considerable difference in sensation compared to unaffected side 2 – all answers are correct, little or no difference	16
Passive joint motion/joint pain	Shoulder Flexion Abduction to 90 degrees Outward rotation Inward rotation Elbow Flexion Extension Forearm Pronation Supination Wrist Flexion Extension Fingers Flexion Extension Hip Flexion Abduction Outward rotation Inward rotation Knee Flexion Extension Ankle Dorsiflexion Plantar-flexion Foot Pronation Supination	0 – only a few degrees range of motion 1 – decreased passive range of motion 2 – normal passive range of motion 0 – pronounced pain during all the movement 1 – some pain 2 – no pain	44 44

1.4 Grip Strength

Measured using dynamometer

Instructions for use

The electronic dynamometer consists of two flat padded bars mounted parallel to each other 2cm apart. When these are squeezed together they maximum force is indicated on a digital display. A standardised position of grip is used. The patient sits with hand resting comfortably in lap. The dynamometer is placed with a marker point on one bar against the cleft between thumb and index finger.

The digital display is set to zero (the patient is not able to see the display). The patient is then asked to squeeze as hard as possible and then release. No encouragement or feedback is given. The procedure is repeated three times, with each hand alternating between affected and unaffected sides.

	Right	**Left**
1		
2		
3		

1.5 Rivermead Motor Assessment

General Instructions

Go through the items in order of difficulty. Score 1 if patient can perform activity, 0 if he cannot. Three tries are allowed. After three consecutive failures, stop that section and proceed to the next. Give no feedback of whether correct or incorrect, just give general encouragement. Repeat instructions and demonstrate them to the patient if necessary. All exercises to be carried out independently unless otherwise stated. All arm tests refer to the affected arm unless otherwise stated.

Score

Gross Function

1. Sit unsupported
   Without holding on, on edge of bed, feet unsupported ☐

2. Lying to sitting on side of bed
   Using any method ☐

3. Sitting to standing
   May use hands to push up. Must stand up in 15 sec and stand for 15 sec,
   With an aid if necessary. ☐

4. Transfer from wheelchair to chair towards unaffected side
   May use hands ☐

5. Transfer from wheelchair to chair towards affected side
   May use hands ☐

6. Walk 10m indoors with an aid
   Any walking aid. No stand-by help. ☐

7. Climb stairs independently
   Any methods. May use banister and aid – must be a full flight of stairs. ☐

8. Walk 10m indoors without an aid
   No stand-by help. No caliper, splint or walking aid. ☐

9. Walk 10m, pick up bean bag from floor, turn and carry back
   Bend down any way, may use aid to walk if necessary. No stand-by help.
   May use either hand to pick up bean bag. ☐

10. Walk outside 40m
    May use walking aid, caliper or splint. No stand-by help. ☐

11. Walk up and down four steps.
    Patient may use an aid if he would normally use one, but may not hold on to a rail. This is included to test ability to negotiate curb or stairs without a rail. ☐

12. Run 10m
    Must be symmetrical. ☐

13. Hop on affected leg five times on the spot
    Must hop on ball of foot without stopping to regain balance.
    No help with arms. ☐

Leg and Trunk

1. Roll to affected side
   Starting position should be lying, not crook lying

2. Roll to unaffected side
   Starting position should be lying, not crook lying

3. Half-bridging
   Starting position – half-crook lying. Patient must put some weight through affected leg to lift hip on affected side. Therapist may position leg, but patient must maintain position even after movement is completed.

4. Sitting to standing
   May not use arms – feet must be flat on floor – must put weight through both feet.

5. Half-crook lying: lift affected leg over side of bed and return it to same position
   Affected leg in half-crook position. Lift leg off bed on to support; for example, box, stool, floor, so that hip is in neutral and knee at 90 degrees while resting on support. Must keep affected knee flexed throughout movement. Do not allow external rotation at hip. This tests control of knee and hip.

6. Standing, step unaffected leg on and off block
   Without retraction of pelvis or hyperextension of knee. This tests knee and hip control while weight bearing through the unaffected leg.

7. Standing, tap ground lightly five times with unaffected foot
   Without retraction of pelvis or hyperextension of knee. Weight must stay on affected leg. This again tests knee and hip control while weight bearing through the affected leg but is more difficult than in 6.

8. Lying, dorsiflex affected ankle with leg flexed
   Physiotherapist may hold affected leg in position, knee at 90 degrees. Do not allow any inversion. Must have half range of movement of unaffected foot.

9. Lying, dorsiflex affected ankle with leg extended
   Same conditions as in 8, with leg extended. Do not allow any inversion or knee flexion. Foot must reach plantigrade (90 degrees).

10. Stand with affected hip in neutral position, flex affected knee
    Therapist may not position leg. This is extremely difficult for most hemiplegic patients, but is included to assess minimal dysfunction.

Score

Arm

1. Lying, protract shoulder girdle with arm in elevation
   Arm may be supported

2. Lying, hold extended arm in elevation (some external rotation) for at least 2 seconds
   Therapist should place arm in position and patient must maintain position with some external rotation. Do not allow pronation. Elbow must be held within 30 degrees of full extension.

3. Flexion and extension of elbow, with arm as in 2 above
   Elbow must extend to at least 20 degrees full extension. Palm should not face outward during any part of movement.

4. Sitting, elbow into side, pronation and supination
   Three-quarters range is acceptable, with elbow unsupported and at right angles.

5. Reach forward, pick up large ball with both hands and place down again
   Ball should be on table so far in front of patient that he has to extend Arms fully to reach it. Shoulders must be protracted, elbows extended, wrists neutral or extended, and fingers extended throughout movement. Palms should be kept in contact with the ball.

6. Stretch arm forward, pick up tennis ball from table, release on mid-thigh on affected side, return to table, then release again on table. Repeat five times.
   Shoulder must be protracted, elbow extended and wrist neutral or extended during each phase.

7. Same exercise as in 6 above with pencil
   Patient must use thumb and fingers to grip.

8. Pick up a piece of paper from table in front and release five times
   Patient must use thumb and fingers to pick up paper and not pull it to edge of table. Arm position as in 6 above.

9. Cut putty with a knife and fork on plate with non-slip mat and put pieces into container at side of plate
   Bite-size pieces

10. Stand on spot, maintain upright position, pat large ball on floor with palm of hand for 5 continuous bounces

11. Continuous opposition of thumb and each finger more than 14 times in 10 sec
    Must do movements in consistent sequence. Do not allow thumb to slide from one finger to the other.

12. Supination and pronation on to palm of affected hand 20 times in 10 sec
    Arm must be away from body, the palm and dorsum of hand must touch palm of good hand. Each tap counts as one. This is similar to 4 above, but introduces speed

Score

13. Standing, with affected arm abducted to 90 degrees with palm flat against wall. Maintain arm in position. Turn body towards wall and as far as possible towards arm i.e. rotate body beyond 90 degrees

    Do not allow flexion at elbow, and wrist must be extended with palm of hand fully in contact with wall.

☐

14. Place string around head and tie bow at back

    Do not allow neck to flex. Affected hand must be used for more than just supporting string. This tests function of hand without help of sight.

☐

15. 'Pat-a-cake' seven times in 15 sec

    Mark crosses on wall at shoulder level. Clap both hands together (both hands touch crosses – clap – one hand touches opposite cross). Must be in correct order. Palms must touch. Each sentence counts as one. Give patient three tries. This is a complex pattern which involves co-ordination, speed, and memory, as well as good arm function.

☐

1.6 Star Cancellation Test

- Place the star chart flat in front of the subject so that the central arrow of the page is in the subject's midline.
- Explain that this is a page full of small stars, big stars and letters.
- You are going to ask them to cross out all the small stars that they can see on the page.
- Demonstrate by crossing out the two small stars immediately above the arrow.
- Give the pen to the subject, or if they are unable to hold the pen ask them to point to the small stars so that you can then cross them out.
- Continue to cross out stars until the subject confirms that they cannot see any more.
- There is no time limit, but do not prompt subject or move the page once it has been put in the midline.

Score : number of stars subject crossed out = _____ (max = 54)

PASS (52 - 54) ☐ **FAIL (0 - 51)** ☐ **UNABLE TO ASSESS** ☐

1.7 Bobath Assessment Chart

Tests for Arm and Shoulder Girdle (to be tested separately in supine, sitting and standing, as the result will be different in these positions).
All to be answered 'Yes' or 'No'

Grade 1

a. Can he hold extended arm in elevation having placed it there?
With internal rotation?
With external rotation?

b. Can he lower the extended arm from the position of elevation to the horizontal plane and back again to elevation?
Forward-downwards?
Sideways-downwards?
With internal rotation?
With external rotation?

c. Can he move the extended abducted arm from the horizontal plane to the side of his body and back again to the horizontal plane?
With internal rotation?
With external rotation?

Grade 2

a. Can he lift his arm to touch the opposite shoulder?
With palm of hand?
With back of hand?

b. Can he bend his elbow with his arm in elevation to touch the top of his head?
With pronation?
With supination?

c. Can he fold his hands behind his head with both elbows in horizontal abduction?
With wrist flexed?
With wrist extended?

Grade 3

a. Can he supinate his forearm and wrist?
Without side-flexion of trunk on the affected side?
With flexed elbow and flexed fingers?
With extended elbow and extended fingers?

b. Can he pronate his forearm without adduction of arm at shoulder?

c. Can he externally rotate his extended arm?
In horizontal abduction?
By the side of the body?
In elevation?

d. Can he bend and extend his elbow in supination to touch the shoulder of the same side?
Starting with:
Arm by sidė of body?
Horizontal abduction of the arm?

Tests for Wrist and Fingers

Grade 1

a. Can he place his flat hand forward down on table in front?
Can he do this sideways when sitting on plinth?
With fingers and thumb adducted?
With fingers and thumb abducted?

Grade 2

a. Can he open his hand to grasp?
With flexed wrist?
With extended wrist?
With pronation?
With supination?
With adducted fingers and thumb?
With abducted fingers and thumb?

Grade 3

a. Can he grasp and open his fingers again?
With flexed elbow?
With extended elbow?
With pronation?
With supination?

b. Can he move individual fingers?
Thumb?
Index finger?
Little finger?
2^{nd} and 3^{rd} finger?

c. Can he oppose fingers and thumb?
Thumb and index finger?
Thumb and 2^{nd} finger?
Thumb and little finger?

1.8 Nine-hole Peg Test

Equipment

- 9 wooden dowels; 9mm diameter, 32mm long.
- Wood base with 9 holes (10mm diameter, 15mm deep) spaced 15mm apart in three rows of three holes.
- Lid to base, with tray 100mm square and 100mm deep to hold pegs.

Instructions

Patient to sit at table, and asked to place pegs in holes. Observer times from start to end, but can stop at 50 sec and record number of pegs placed.

Results

Best presented as number of seconds taken to place each peg.

1.9 Box and Block Test

A box with a partition directly in the centre, creating two equal sides, is used for this test. A number of small wooden blocks are placed in one side of the box.

The subject is required to use their dominant had to grasp one block at a time and transport it over the partition and release it into the opposite side. The subject is given 60 seconds in which to complete the test, and the number of blocks transported to the other side is counted. The test is then repeated with the non-dominant hand.

1.10 Frenchay Arm Test

Instructions

The patient sits at a table with his/her hands on his/her lap. Each task starts from this position. The patient scores one for each task completed successfully (and nought if he/she fails), and is asked to use each hand to:

	R	L
1. Stabilise a ruler while drawing a line with a pencil held in the other hand. To pass, the ruler must be held firmly.	☐	☐
2. Grasp a cylinder (12mm diameter, 5cm long) set on its end approximately 15cm from the table edge, lift it about 30cm and replace it without dropping.	☐	☐
3. Pick up a glass half-full of water positioned 15-30cm from the table edge, drink some water and replace the glass without spilling any water.	☐	☐
4. Remove and replace a sprung clothes peg from a 10mm diameter dowel, 15cm long, set in a 10cm square base, placed 15-30cm from the table edge. He/she is not to drop the peg or knock the dowel over.	☐	☐
5. Comb his/her hair (or imitate); he/she must comb across the top, down the back and down each side of the head.	☐	☐

TOTAL SCORES:

RIGHT ☐ **LEFT** ☐

1.11 Action Research Arm Test

Instructions - There are four subtests: grasp, grip, pinch and gross movement.
If a subject passes the first the first task in each subtest then they score top marks and move onto the next subtest. If a subject fails the first and the second task in a subtest, then they score zero overall for that subtest and move onto the next. The patient must be able to sit unaided in order to attempt the test. If not, the patient scores 0.

Score 0 = can perform no part of the test
1 = performs test partially
2 = completes test, but takes abnormally long time
3 = performs test normally

ARAT done
unable to sit (score 0)
ARAT not done (score missing value)
(Give reason _____)

Start with the least impaired arm first

	R	L
a) Grasp		
10cm cube (if score = 3 then total = 18 & go to *Grip*)		
1. 2.5cm cube (if Grasp score = 0 so far then Grasp total = 0 & go to *Grip*)		
2. 5cm cube		
3. 7.5cm cube		
4. cricket ball		
5. stone		
Grasp total:		
b) Grip		
1. Pour water glass to glass (if score = 3 then total = 12 & go to *Pinch*)		
2. 2.25cm tube (if Grip score = 0 so far then Grip total = 0 & go to *Pinch*)		
3. 1cm tube		
4. washer over bolt		
Grip total:		
c) Pinch		
1. 6mm bearing 3rd finger & thumb (if score = 3 then total = 18 & go to *Gross*)		
2. marble index & thumb (if Pinch score = 0 so far then Pinch total = 0 & go to *Gross*)		
3. 6mm bearing 2nd finger & thumb		
4. 6mm bearing 1st finger & thumb		
5. marble 2nd finger & thumb		
6. marble 3rd finger & thumb		
Pinch total:		
d) Gross		
1. Place hand behind head (if score = 3 then total = 9 & finish)		
2. Place hand on top of head		
3. Hand to mouth		
Gross total:		
ARAT Total		

1.12 Barthel Activities of Daily Living Index

Function	Description	Score	
Bowels	Incontinent (or needs to be given enema) Occasional accidence (once a week) Continent	0 1 2	
Bladder	Incontinent, or catheterised and unable to manage Occasional accident (max. once per 24 hours) Continent (for more than 7 days)	0 1 2	
Grooming	Needs help with personal care: face, hair, teeth, shaving Independent (implements provided)	0 1	
Toilet Use	Dependent Needs some help but can do some things alone Independent (one and off, wiping, dressing)	0 1 2	
Feeding	Unable Needs help in cutting, spreading butter etc. Independent (food provided within reach)	0 1 2	
Transfer	Unable - no sitting balance Major help (physical, 1 or 2 people), can sit Minor help (verbal or physical) Independent	0 1 2 3	
Mobility	Immobile Wheelchair independent, including corners etc. Walks with help of one person (verbal or physical) Independent	0 1 2 3	
Dressing	Dependent Needs help but can do about half unaided Independent (including buttons, zips, laces etc.)	0 1 2	
Stairs	Unable Needs help (verbal, physical, carrying aid) Independent up and down	0 1 2	
Bathing	Dependent Independent (Bath: must get in and out unsupervised and wash self. Shower: unsupervised/unaided).	0 1	
Total (0-20)			

1.13 Rivermead Activities of Daily Living Scale

Instructions

1. Decide where to start. If the patient can do that item, go back three to make sure that the patient can do these as well, and forward until three consecutive failures – then stop. This applies to each section.
2. All aids supplied or recommended to be stated on form.
3. Guidelines are given on next page.

Scoring

3 = Independent with/without aid
2 = Verbal assistance only
1 = Dependent (i.e. if unfit, un-assessable, unsafe or time taken is beyond practical bounds)

Item	Score	Equipment
Self care		
Drinking		
Clean teeth		
Comb hair		
Wash face/hands		
Make up or shave		
Eating		
Undress		
Indoor mobility		
Bed to chair		
Lavatory		
Outdoor mobility		
Dressing		
Wash in bath		
In/out bath		
Overall wash		
Floor to chair		
Household 1		
Preparation of hot drink		
Preparation of snack		
Cope with money		
Get in/out car		
Prepare meal		
Carry shopping		
Crossing roads		
Transport self to shop		
Public transport		
Household 2		
Washing		
Ironing		
Light cleaning		
Hang out washing		
Bed making		
Heavy cleaning		

1.14 Nottingham Extended Activities of Daily Living Index

Before your recent stroke, were you living alone? No ☐ Yes ☐ Don't know ☐

	Not at all	***With help***	***Alone with difficulty***	***Alone easily***
a) Mobility				
In the month before your stroke, did you:				
• walk around outside?	☐	☐	☐	☐
• climb stairs?	☐	☐	☐	☐
• get in and out of the car?	☐	☐	☐	☐
• walk over uneven ground?	☐	☐	☐	☐
• cross roads?	☐	☐	☐	☐
• travel on public transport?	☐	☐	☐	☐
b) In the kitchen				
In the month before your stroke, did you:				
• manage to feed yourself?	☐	☐	☐	☐
• manage to make yourself a hot drink?	☐	☐	☐	☐
• take hot drinks from one room to another?	☐	☐	☐	☐
• do the washing up?	☐	☐	☐	☐
• make yourself a hot snack?	☐	☐	☐	☐
c) Domestic tasks				
In the month before your stroke, did you:				
• manage your own money when you were out?	☐	☐	☐	☐
• wash small items of clothing?	☐	☐	☐	☐
• do your own shopping?	☐	☐	☐	☐
• do your own housework?	☐	☐	☐	☐
• do a full clothes wash?	☐	☐	☐	☐
d) Leisure Activities				
In the month before your stroke, did you:				
• read newspapers or books?	☐	☐	☐	☐
• use the telephone?	☐	☐	☐	☐
• write letters?	☐	☐	☐	☐
• go out socially?	☐	☐	☐	☐
• manage your own garden?	☐	☐	☐	☐
• drive a car?	☐	☐	☐	☐

Scoring 0= Not at all 1 = With help 2 = On my own with difficulty 3 = Alone easily

1.15 Functional Independence Measure and Functional Assessment Measure

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Scale:

7 Complete Independence (timely, safely)
6 Modified Independence (extra time, devices)
5 Supervision (cuing, coaxing, prompting)
4 Minimal Assist (performs 75% or more of task)
3 Moderate Assist (performs 50-74% of task)
2 Maximal Assist (performs 25-49% of task)
1 Total Assist (performs less than 25% of task)

Self Care Items

1. Feeding
2. Grooming
3. Bathing
4. Dressing upper body
5. Dressing lower body
6. Toileting
7. Swallowing*

Sphincter Control

8. Bladder management
9. Bowel management

Mobility items (Type of transfer)

10. Bed, chair, wheelchair
11. Toilet
12. Bath or shower
13. Car transfer*

Locomotion

14. Walking/wheelchair (circle)
15. Stairs
16. Community access*

Communication items

17. Comprehension – audio/visual (circle)
18. Expression – verbal, non-verbal (circle)
19. Reading*
20. Writing*
21. Speech intelligibility*

Psychosocial adjustment

22. Social interaction
23. Emotional status*
24. Adjustment to limitations*
25. Employability*

Cognitive function

26. Problem solving
27. Memory
28. Orientation*
29. Attention*
30. Safety judgement*

* FAM items

1.16 Frenchay Activities Index

Score	Activity	Code (score)
	In the last three months	
_____	Preparing main meals	0 = Never 1 = Under once weekly 2 = 1-2 times/week 3 = Most days
_____	Washing up	
_____	Washing clothes	0 = Never 1 = 1-2 times in three months 2 = 3=12 times in three months 3 = At least weekly
_____	Light housework	
_____	Heavy housework	
_____	Local shopping	
_____	Social occasions	
_____	Walking outside >15 mins	
_____	Actively pursuing hobby	
_____	Driving car/going on bus	
	In last six months	
_____	Travel outings/car rides	0 = never 1 = 1-2 times in 6 months 2 = 3-12 times in 6 months 3 = At least twice weekly
_____	Gardening	0 = Never 1 = Light 2 = Moderate 3 = All necessary
_____	Household/car maintenance	
_____	Reading books	0 = None 1 = One in 6 months 2 = Less than one in a fortnight 3 = Over one each fortnight
_____	Gainful work	0 = None 1 = Up to 10 hours/week 2 = 10-30 hours/week 3 = Over 30 hours/week

1.17 Motor Assessment Scale

General instructions

1. The test should preferably be carried out in a quiet private room or curtained-off area.

2. The test should be carried out when the patient is maximally alert and not when under the influence of hypnotic or sedative drugs. Record if the patient is under the influence of sedative drugs.

3. Patient should be dressed in suitable street clothes with sleeves rolled up and without shoes and socks. Items 1 to 3 inclusive may be scored if necessary with the patient in his right clothes.

4. Each item is recorded on a scale of 0 to 6.

5. All items are to be performed independently by the patient unless otherwise stated. 'Stand-by help' means that the physical therapist stands by and may steady patient but must not actively assist.

6. Items 1 to 8 are recorded according to the patient's responses to specific instructions. General Tonus (item 9) is scored from continuous observations and handling throughout the assessment.

7. Patient should be scored on best performance. Repeat three times unless other specific instructions are given.

8. Because the scale is designed to score the patient's best performance, the physical therapist should give general encouragement but should not give specific feedback on whether response is correct or incorrect. Sensitivity to the patient is necessary to enable him to produce his best performance.

9. Instructions should be repeated and demonstrations given to the patient if necessary.

10. The order of administration of the items can be varied according to convenience.

11. If the patient becomes emotionally labile at any stage during scoring, the physical therapist should wait 15 sec before attempting the following procedures:
    - ask patient to close his mouth and take a deep breath; and
    - hold the patient's jaw closed and ask the patient to stop crying.

    If patient is unable to control behaviour, the examiner should cease testing him and re-score this item and any other items unscored at a more suitable time.

12. If performance is scored differently on left and right side, the physical therapist may indicate this with an 'L' in one box and an 'R' in another box.

13. The patient should be informed when being times.

14. You will need: a low, wide plinth, a stopwatch, a polystyrene cup, eight jelly-beans, two teacups, a rubber ball 14cm (5 in) in diameter, a stool, a comb, a top of a pen, a table, a dessert spoon and water, a pen, a prepared sheet for drawing lines, and a cylindrical object such as a jar.

A. ***Supine to side lying on to intact side***

1. Pulls himself into side lying
   Starting position must be supine lying, not knees flexed. Patient pulls himself into side lying with intact arm, moves affected leg with intact leg.

2. Moves leg across actively and lower half of body follows
   Starting position as above. Arm is left behind.

3. Arm is lifted across body with other arm. Leg is moved actively and body follows in a block.
   Starting position as above.

4. Moves arm across body actively and rest of body follows in a block.
   Starting position as above.

5. Moves arm and leg and rolls to side but overbalances
   Starting position as above. Shoulder protracts and arm flexes forward.

6. Rolls to side in 3 sec
   Starting position as above. Must not use hands.

B. ***Supine to sitting over side of bed***

1. Side lying, lifts head sideways but cannot sit up
   Patient assisted to side lying.

2. Side lying to sitting over side of bed
   Therapist assists patient with movement. Patient controls head position throughout.

3. Side lying to sitting over side of bed.
   Therapist gives stand-by help by assisting legs over side of bed.

4. Side lying to sitting over side of bed
   With no stand-by help.

5. Supine to sitting over side of bed
   With no stand-by help.

6. Supine to sitting over side of bed within 10 sec
   With no stand-by help.

C. ***Balanced sitting***

1. Sits only with support
   Therapist should assist patient into sitting.

2. Sits unsupported for 10 sec
   Without holding on, knees and feet together, feet can be supported on floor

3. Sits unsupported with weight well forward and evenly distributed
   Weight should be well forward at the hips, head and thoracic spine extended, weight evenly distributed on both sides.

4. Sits unsupported, turns head and trunk to look behind
   Feet supported and together on floor. Do not allow legs to abduct or foot to move. Have hands resting on thighs, do not allow hands to move on to plinth.

5. Sits unsupported, reaches forward to touch floor, and returns to starting position.
   Feet supported on floor. Do not allow patient to hold on. Do not allow legs and feet to move, support affected arm if necessary. Hand must touch floor at least 10cm (4 in) in front of feet.

6. Sits on stool unsupported, reaches sideways to touch floor, and returns to starting position.
   Feet supported on floor. Do not allow patient to hold on. Do not allow legs and feet to move, support affected arm if necessary. Patient must reach sideways, not forward.

D. ***Sitting to standing***

1. Gets to standing position with help from therapist.
   Any method.

2. Gets to standing position with stand-by help.
   Weight unevenly distributed, uses hands for support.

3. Gets to standing position
   Do not allow uneven weight distribution or help from hands.

4. Gets to standing position and stands for 5 sec with hips and knees extended.
   Do not allow uneven weight distribution.

5. Sitting to standing with no stand-by help.
   Do not allow uneven weight distribution. Full extension of hips and knees.

6. Sitting to standing with no stand-by help three times in 10 sec.
   Do not allow uneven weight distribution.

E. ***Walking***

1. Stands on affected leg and steps forward with other leg.
   Weight-bearing hip must be extended. Therapist may give stand-by help.

2. Walks with stand-by help from one person.

3. Walks 3m (10 ft) along or uses any aid but no stand-by help.

4. Walks 5m (16 ft) with no aid in 15 sec.

5. Walks 10m (33 ft) with no aid, turns around, picks up a small sandbag from floor, and walks back in 25 sec.
   May use either hand.

6. Walks up and down four steps with or without an aid but without holding on to the rail three times in 35 sec.

F. ***Upper-arm function***

1. Lying, protract shoulder girdle with arm in elevation.
   Therapist places arm in position and supports it with elbow in extension.

2. Lying, hold extended arm in elevation for 2 sec.
   Therapist should place arm in position and patient must maintain position with some external rotation. Elbow must be within 20 degrees of full extension.

3. Flexion and extension of elbow to take palm to forehead with arm as in 2 above.
   Therapist may assist supination of forearm.

4. Sitting, hold extended arm in forward flexion at 90 degrees to body for 2 sec.
   Therapist should place arm in position and patient must maintain position with some external rotation and elbow extension. Do not allow excess shoulder elevation.

5. Sitting, patient lifts arm to above position, holds it there for 10 seconds, and then lowers it.
   Patient must maintain position with some external rotation. Do not allow pronation.

6. Standing, hand against wall. Maintain arm position while turning body towards wall.
   Have arm abducted to 90 degrees with palm flat against the wall.

G. *Hand movements*

1. Sitting, extension of the wrist.
   Therapist should have patient sitting at table with forearm resting on the table. Therapist places cylindrical object in palm of patient's hand. Patient is asked to lift object off the table by extending the wrist. Do not allow elbow flexion.

2. Sitting, radial deviation of wrist.
   Therapist should place forearm in mid-pronation-supination (i.e. resting on ulnar side, thumb in line with forearm and wrist in extension, fingers around a cylindrical object). Patient asked to lift hand off table. Do not allow elbow flexion or pronation.

3. Sitting, elbow into side, pronation and supination.
   Elbow unsupported and at a right angle. Three-quarter range is acceptable.

4. Reach forward, pick up large ball of 14 cm (5-in) diameter with both hands and put it down.
   Ball should be on table so far in front of patient who has to extend arms fully to reach it. Shoulders must be protracted, elbows extended, wrist neutral or extended. Palms should be kept in contact with the ball.

5. Pick up a polystyrene cup from table and put it on table across other side of body.
   Do not allow alteration in shape of cup.

6. Continuous opposition of thumb and each finger more than 14 times in 10 sec.
   Each finger in turn taps the thumb, starting with index finger. Do not allow thumb to slide from one finger to the other, or to go backwards.

H. *Advanced hand activities*

1. Picking up the top of a pen and putting it down again.
   Patient stretches arm forward, picks up pen top, releases it on table close to body.

2. Picking up one jellybean from a cup and placing it in another cup.
   Teacup contains eight jellybeans. Both cups must be at arms length. Left hand takes jellybean from cup on right and releases it in cup on left.

3. Drawing horizontal lines to stop at a vertical line 10 times in 20 sec
   At least five lines must touch and stop at the vertical line.

4. Holding a pencil, making rapid consecutive dots on a sheet of paper.
   Patient must do at least two dots a second for 5 sec. Patient picks pencil up and positions it without assistance. Patient must hold pen as for writing. Patient must make a dot and not a stroke.

5. Taking a dessert spoon of liquid to the mouth.
   Do not allow head to lower towards spoon. Do not allow liquid to spill.

6. Holding a comb and combing hair at back of head.

I. ***General tonus***

1. Flaccid, limp, no resistance when body parts are handled.

2. Some response felt as body parts are moved.

3. Variable, sometimes flaccid, sometimes good tone, sometimes hypertonic.

4. Consistently normal response.

5. Hypertonic 50 per cent of the time.

6. Hypertonic at all times.

1.18 Health Assessment Questionnaire

We are interested in learning how your illness affects your ability to function in daily life. Please feel free to add any comments at the end of this form. Please choose from the answers given.
Answers
0 = without *any* difficulty 1 = with *some* difficulty 2 = with *much* difficulty 3 = unable to do

Item	Answer (score)
1. *Dressing and grooming* Are you able to: • dress yourself, including tying shoelaces and doing-up buttons? • shampoo your hair?	_____ _____
2. *Rising* Are you able to: • stand up from an armless straight chair? • get in and out of bed?	_____ _____
3. *Eating* Are you able to: • cut your meat? • lift a full cup or glass to your mouth? • open a new carton of milk (or soap powder)?	_____ _____ _____
4. *Walking* Are you able to: • walk outdoors on flat ground? • climb up five steps?	_____ _____
5. *Hygiene* Are you able to: • wash and dry your entire body? • take a bath? • get on and off the toilet?	_____ _____ _____
6. *Reach* Are you able to: • reach and get down a 5 lb (2 kg) object from above your head (for example, a bag of potatoes)? • bend down and pick up clothing from the floor?	_____ _____
7. *Grip* Are you able to: • open car doors? • open jars which have been previously opened? • turn taps (faucets) on and off?	_____ _____ _____
8. *Activities* Are you able to: • run errands and go shopping? • get in and out of the car? • do chores such as vacuuming, housework, or light gardening?	_____ _____ _____

1.19 The Modified Rankin Scale

0	No symptoms at all	☐
1	No significant disability despite symptoms able to carry out all usual duties and activities	☐
2	Slight disability; unable to carry out all previous activities, but still able to look after own affairs without assistance	☐
3	Moderate disability; requiring some help	☐
4	Moderately severe disability; needing help but not so bad as to need attention day and night	☐
5	Severe disability; requiring constant attention	☐

1.20 Nottingham Health Profile

Listed below are some problems that people might have in their daily lives. Please read the list carefully and put a tick in the box 3 under Yes for any problem that applies to you at the moment. Tick the box under No for any problem that does not apply to you. PLEASE TRY TO ANSWER EVERY QUESTION. If you are not sure whether to answer Yes or No, tick whichever answer you think is MOST true at the moment.

		No	Yes
0)	I'm tired all the time	☐	☐
1)	I have pain at night	☐	☐
2)	Things are getting me down	☐	☐
3)	I have unbearable pain	☐	☐
4)	I take tablets to help me sleep	☐	☐
5)	I've forgotten what it's like to enjoy myself	☐	☐
6)	I'm feeling on edge	☐	☐
7)	I find it painful to change position	☐	☐
8)	I feel lonely	☐	☐
9)	I can only walk about indoors	☐	☐
10)	I find it hard to bend	☐	☐
11)	Everything is an effort	☐	☐
12)	I'm waking up in the early hours of the morning	☐	☐
13)	I'm unable to walk at all	☐	☐
14)	I'm finding it hard to make contact with people	☐	☐

		No	Yes
15)	The days seem to drag	☐	☐
16)	I have trouble getting up and down stairs or steps	☐	☐
17)	I find it hard to reach for things	☐	☐
18)	I'm in pain when I walk	☐	☐
19)	I lose my temper easily these days	☐	☐
20)	I feel there is nobody I am close to	☐	☐
21)	I lie awake for most of the night	☐	☐
22)	I feel as if I'm losing control	☐	☐
23)	I'm in pain when I'm standing	☐	☐
24)	I find it hard to dress myself	☐	☐
25)	I soon run out of energy	☐	☐
26)	I find it hard to stand for long (e.g. at the kitchen sink or waiting for a bus)	☐	☐
27)	I'm in constant pain	☐	☐
28)	It takes me a long time to get to sleep	☐	☐
29)	I feel I am a burden to people	☐	☐
30)	Worry is keeping me awake at night	☐	☐
31)	I feel that life is not worth living	☐	☐
32)	I sleep badly at night	☐	☐
33)	I'm finding it hard to get on with people	☐	☐

		No	Yes
34)	I need help to walk about outside (e.g. a walking aid or someone to support me)	☐	☐
35)	I'm in pain when going up and down stairs or steps	☐	☐
36)	I wake up feeling depressed	☐	☐
37)	I'm in pain when I'm sitting	☐	☐

1.21 Health Status Questionnaire (SF-36)

The following questions ask for your views about your health, how you feel and how well you are able to do your usual activities.

If you are unsure about how to answer a question, please give the best answer you can and make any comments in the space available at the end of the questionnaire.

1. In general, would you say your health is:

	(Circle one)
Excellent	1
Very good	2
Good	3
Fair	4
Poor	5

2. Compared to three months ago, how would you rate your health in general now?

	(Circle one)
Much better than 3 months ago	1
Somewhat better than 3 months ago	2
About the same	3
Somewhat worse now than 3 months ago	4
Much worse now than 3 months ago	5

HEALTH AND DAILY ACTIVITIES

3. The following questions are about activities that you might do during a typical day. Does your health limit you in these activities? If so, how much? **(Circle one number on each line)**

	ACTIVITIES	Yes, limited a lot	Yes, limited a little	No, not limited at all
a	**Vigorous activities**, such as running, lifting heavy objects, participating in strenuous sports	1	2	3
b	**Moderate activities**, such as moving a table, pushing a vacuum cleaner, bowling or playing golf	1	2	3
c	Lifting or carrying groceries	1	2	3
d	Climbing **several** flights of stairs	1	2	3
e	Climbing **one** flight of stairs	1	2	3
f	Bending, kneeling or stooping	1	2	3
g	Walking **more than a mile**	1	2	3
h	Walking **half a mile**	1	2	3
i	Walking **100 yards**	1	2	3
j	Bathing or dressing yourself	1	2	3

4. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

(Circle one number on each line)

		Yes	No
a	Cut down on the **amount of time** you spent on work or other activities	1	2
b	**Accomplished less** than you would like	1	2
c	Were limited in the **kind** of work or other activities	1	2
d	Had **difficulty** in performing the work or other activities (e.g. it took extra effort)	1	2

5. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

(Circle one number on each line)

		Yes	No
a	Cut down on the **amount of time** you spent on work or other activities	1	2
b	**Accomplished less** than you would like	1	2
c	Didn't do work or other activities as **carefully** as usual	1	2

6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours or groups?

	(Circle one)
Not at all	1
Slightly	2
Moderately	3
Quite a bit	4
Extremely	5

7. How much bodily pain have you had during the past 4 weeks?

	(Circle one)
None	1
Very mild	2
Mild	3
Moderate	4
Severe	5
Very severe	6

8. During the past 4 weeks, how much did pain interfere with your normal work (including work both outside the home and housework)?

	(Circle one)
Not at all	1
A little bit	2
Moderately	3
Quite a bit	4
Extremely	5

YOUR FEELINGS

9. These questions are about how you feel and how things have been with you during the past 4 weeks. (For each question, please indicate the one answer that comes closest to the way you have been feeling).

(Circle one number on each line)

	How much of the time during the past 4 weeks:	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
a	Did you feel full of life?	1	2	3	4	5	6
b	Have you been a very nervous person?	1	2	3	4	5	6
c	Have you felt so down in the dumps that nothing could cheer you up?	1	2	3	4	5	6
d	Have you felt calm and peaceful?	1	2	3	4	5	6
e	Did you have a lot of energy?	1	2	3	4	5	6
f	Have you felt down-hearted and low?	1	2	3	4	5	6
g	Did you feel worn-out?	1	2	3	4	5	6
h	Have you been a happy person?	1	2	3	4	5	6
i	Did you feel tired?	1	2	3	4	5	6
j	Has your health limited your social activities (like visiting friends or close relatives)	1	2	3	4	5	6

10. Please choose the answer that best describes how true or false each of the following statements is for you?

(Circle one number on each line)

		Definitely true	Mostly true	Not sure	Mostly false	Definitely false
a	I seem to get ill more easily than other people	1	2	3	4	5
b	I am as healthy as anybody I know	1	2	3	4	5
c	I expect my health to get worse	1	2	3	4	5
d	My health is excellent	1	2	3	4	5

Comments

1.22 Stroke Specific Quality of Life Scale

Response Set Key

1.	Total help **1**	A lot of help **2**	Some help **3**	A little help **4**	No help needed **5**
2.	Couldn't do it at all **1**	A lot of trouble **2**	Some trouble **3**	A little trouble **4**	No trouble at all **5**
3.	Strongly agree **1**	Moderately agree **2**	Neither agree nor disagree **3**	Moderately disagree **4**	Strongly disagree **5**

Item		Response Set
Energy		
1.	I spent a lot of time in bed	3
2.	I felt tired most of the time	3
3.	I had to stop and rest often during the day	3
4.	I was too tired to do what I wanted to do	3
Family Roles		
1.	Did you need help to do regular daily work around the house?	1
2.	Did you have to stop and rest when you were working around the house?	2
3.	Did you need help to do the shopping?	1
4.	Did you need help taking care of personal jobs, for example, paying bills, going to the bank, making appointments?	1
5.	I didn't join in activities just for fun with my family	3
6.	Did someone else have to drive you around?	2
7.	I felt I was a burden to my family	3
8.	My physical condition interfered with my family life	3
Language		
1.	Did you have trouble communicating, for example, need to use gestures or pointing?	2

1.23 Stroke Impact Scale

The purpose of this questionnaire is to evaluate how stroke has impacted your health and life. We want to know from YOUR POINT OF VIEW how stroke has affected you. We will ask you questions about impairments and disabilities caused by your stroke, as well as how stroke has affected your quality of life. Finally, we will ask you to rate how much you think you have recovered from your stroke.

These questions are about the physical problems that may have occurred as a result of your stroke.

1. In the past week, how would you rate the strength of your.....	A lot of strength	Quite a bit of strength	Some strength	A little strength	No strength at all
a. Arm that was *most affected* by your stroke?	5	4	3	2	1
b. Grip of your hand that was *most affected* by your stroke?	5	4	3	2	1
c. Leg that was *most affected* by your stroke?	5	4	3	2	1
d. Foot/ankle that was *most affected* by your stroke?	5	4	3	2	1

These questions are about your memory and thinking.

2. In the past week, how difficult was it to.....	Not difficult at all	A little difficult	Somewhat difficult	Very difficult	Extremely difficult
a. Remember things that people just told you?	5	4	3	2	1
b. Remember things that happened yesterday?	5	4	3	2	1
c. Remember to do things (e.g. keep scheduled appointments or take medication?)	5	4	3	2	1
d. Remember the day of the week?	5	4	3	2	1
e. Add and subtract numbers?	5	4	3	2	1
f. Concentrate?	5	4	3	2	1
g. Think quickly?	5	4	3	2	1
h. Solve problems?	5	4	3	2	1

These questions are about how you feel, about changes in your mood and your ability to control your emotions since your stroke.

3. In the past week, how often did you.....	None of the time	A little of the time	Some of the time	Most of the time	All of the time
a. Feel sad?	5	4	3	2	1
b. Feel that there is nobody you are close to?	5	4	3	2	1
c. Feel that you are a burden to others?	5	4	3	2	1
d. Feel that you have nothing to look forward to?	5	4	3	2	1
e. Blame yourself for mistakes?	5	4	3	2	1
f. Enjoy things as much as you ever have?	5	4	3	2	1
g. Feel quite nervous?	5	4	3	2	1
h. Feel that life is worth living?	5	4	3	2	1
i. Smile and laugh at least once a day?	5	4	3	2	1

The following items are about your ability to communicate with other people, as well as your ability to understand what you read and what you hear in a conversation.

4. In the past week, how difficult was it to...	Not difficult at all	A little difficult	Somewhat difficult	Very difficult	Extremely difficult
a. Say the name of someone whose face was in front of you?	5	4	3	2	1
b. Understand what was being said to you in a conversation?	5	4	3	2	1
c. Reply to questions?	5	4	3	2	1
d. Correctly name objects?	5	4	3	2	1
e. Participate in a conversation with a group of people?	5	4	3	2	1
f. Have a conversation on the telephone?	5	4	3	2	1
g. Call another person on the telephone (select correct phone number and dial)?	5	4	3	2	1

The following items ask about activities you might do during a typical day.

5. In the past 2 weeks, how difficult was it to...	Not difficult at all	A little difficult	Somewhat difficult	Very difficult	Extremely difficult
a. Cut your food with a knife and fork?	5	4	3	2	1
b. Dress the top part (waist up) of your body?	5	4	3	2	1
c. Bathe yourself?	5	4	3	2	1
d. Clip your toenails?	5	4	3	2	1
e. Get to the toilet on time?	5	4	3	2	1
f. Control your bladder (not have an accident)?	5	4	3	2	1
g. Control your bowels (not have an accident)?	5	4	3	2	1
h. Do light household tasks/chores (e.g. dust, make a bed, take out rubbish, do the dishes)?	5	4	3	2	1
i. Go shopping?	5	4	3	2	1
j. Handle money (e.g. make change)?	5	4	3	2	1
k. Manage finances (e.g. pay monthly bills, manage current account)?	5	4	3	2	1
l. Do heavy household chores (e.g. vacuum, laundry or garden work)?	5	4	3	2	1

The following questions are about your ability to be mobile, at home and in the community.

6. In the past 2 weeks, how difficult was it to....	Not difficult at all	A little difficult	Somewhat difficult	Very difficult	Extremely difficult
a. Sit without losing your balance?	5	4	3	2	1
b. Stand without losing your balance?	5	4	3	2	1
c. Walk without losing your balance?	5	4	3	2	1
d. Move from a bed to a chair?	5	4	3	2	1
e. Get out of a chair without using your hands for support?	5	4	3	2	1
f. Walk down one street?	5	4	3	2	1
g. Walk fast?	5	4	3	2	1
h. Climb one flight of stairs?	5	4	3	2	1
i. Climb several flights of stairs?	5	4	3	2	1
j. Get in and out of a car?	5	4	3	2	1

The following questions are about your ability to use your hand that was MOST AFFECTED by your stroke.

7. In the past 2 weeks, how difficult was it to use your hand that was most affected by your stroke to.....	Not difficult at all	A little difficult	Somewhat difficult	Very difficult	Extremely difficult
a. Carry heavy objects (e.g. bag of groceries)?	5	4	3	2	1
b. Turn a doorknob?	5	4	3	2	1
c. Open a can or jar?	5	4	3	2	1
d. Tie a shoelace?	5	4	3	2	1
e. Pick up a coin?	5	4	3	2	1

The following questions are about how stroke has affected your ability to participate in the activities that you usually do, things that are meaningful to you and help you to find purpose in life.

8. During the past 4 weeks, how much of the time have you been limited in....	None of the time	A little of the time	Some of the time	Most of the time	All of the time
a. Your work, volunteer or other activities?	5	4	3	2	1
b. Your social activities?	5	4	3	2	1
c. Quiet recreation (crafts, reading)?	5	4	3	2	1
d. Active recreation (sports, outings, travel)?	5	4	3	2	1
e. Your role as a family member and/or friend?	5	4	3	2	1
f. Your participation in spiritual or religious activities?	5	4	3	2	1
g. Your ability to feel emotionally connected to another person?	5	4	3	2	1
h. Your ability to control your life as you wish?	5	4	3	2	1
I. Your ability to help others in need?	5	4	3	2	1

9. Stroke Recovery

On a scale of 0 to 100, with 100 representing full recovery and 0 representing no recovery, how much have you recovered from your stroke?

100		Fully recovered
90		
80		
70		
60		
50		
40		
30		
20		
10		
0		Experienced no recovery

1.24 EuroQol EQ-5D Questionnaire

By placing a tick in one box in each group below, please indicate which statement best describes your own health state today.
Do not tick more than one box in each group.

Mobility

I have no problems walking about	☐
I have some problems walking about	☐
I am confined to bed	☐

Self-care

I have no problems with self-care	☐
I have some problems washing or dressing myself	☐
I am unable to wash or dress myself	☐

Usual activities (e.g. work, study, housework, family or leisure activities)

I have no problems with performing my usual activities	☐
I have some problems with performing my usual activities	☐
I am unable to perform my usual activities	☐

Pain/Discomfort

I have no pain or discomfort	☐
I have moderate pain or discomfort	☐
I have extreme pain or discomfort	☐

Anxiety/Depression

I am not anxious or depressed	☐
I am moderately anxious or depressed	☐
I am extremely anxious or depressed	☐

To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked by 0. We would like you to indicate on this scale how good or bad your own health is today, in your opinion. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your health state is.

Worst imaginable health state 0 _____ 100 Best imaginable health state

1.25 5-point Severity Scale and 0-10 Numerical Rating Scale

Do you have pain
in your arms most days? No ☐ Yes ☐

If yes, which arm(s) has been painful? R ☐ L ☐ Both ☐

How would you describe this pain (mark one only)?

Excruciating (very severe)
Severe
Moderate
Mild
None

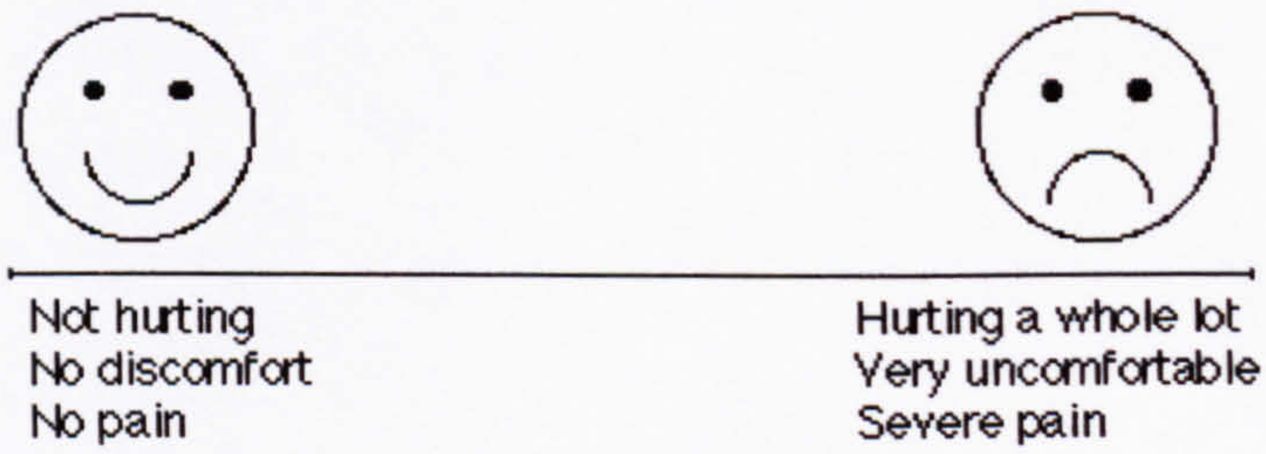
If 0 (zero) is no pain at all, and the number 10 (ten) means as painful as it could be, then how painful was it?
(please give a number between one and ten)

_____

1.26 Visual Analogue Scale

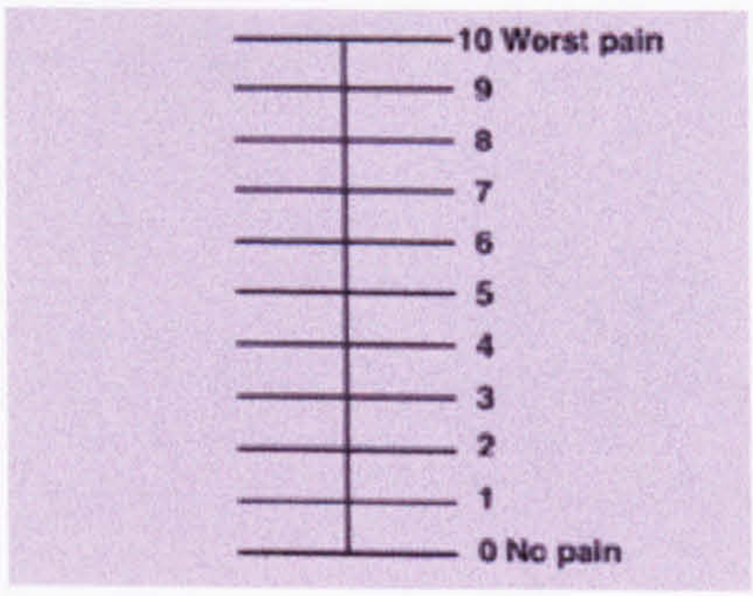
Horizontal visual analogue scale

If the right hand end of the line is as painful as could be, and the left hand end is no pain, please mark on the line where your shoulder pain would be.



Vertical visual analogue scale

If the top of the line is as painful as could be, and the bottom end is no pain, please mark on the line where your shoulder pain would be.



1.27 Upper Extremity Functioning Test

This tests the subjects' ability to perform typical daily activities.

1. Combing hair
2. Using a fork
3. Picking up a VHS (Video Home System) format videotape
4. Picking up a full juice can (volume 0.33 litres)
5. Picking up a full bottle (volume 0.33 litres)
6. Writing with a pen
7. Using the telephone receiver
8. Brushing teeth
9. Pouring from a 1 litre juice box
10. Drinking from a mug (volume 0.25 litres)
11. Handling finger food

The activities include palmar grasp (tasks 4, 5, 7, and 9), lateral grasp (tasks 1, 2, 3 ,8, and 10), and precision grip (tasks 6 and 11). The test evaluates the ability to handle small objects (tasks 1, 2, 5, 6, 8, 10, and 11), large objects (tasks 3, 4, 7, and 9), light objects (tasks 1, 2, 3, 6, 8, and 11), and heavy objects (tasks 4, 5, 7, 9, and 10).

The UEFT score is the number of successful repetitions of a task that a subject can perform during a 2 minute period. A successful operation is one in which the subject grasped, manipulated, and used the object with his or her paretic arm.

1.28 Drawing Test

This measures the subject's ability to coordinate shoulder and elbow movements when the hand is moving in the horizontal plane within the typical workspace.

Subjects are asked to track a square (20cm x 20cm) with their paretic hand. They are instructed not to move their trunk and shoulder during the drawing.

The outcome measure is the ratio between the surface area surrounded by the drawn line and the surface of the square expressed as a percent. The time needed to draw the square is also calculated.

1.29 Modified Ashworth Scale

Positioning:

- The patient is examined sitting in a relaxed position
- The patient's shoulder joint is in 90° abduction or less, depending on patient comfort
- The patient's elbow joint is flexed
- The patient's forearm is supported distally
- The patient's upper arm is stabilised proximal to the elbow
- The patient's forearm is in neutral position in terms of pronation/supination

Ashworth Scale Scoring

	No increase in muscle tone
1	Slight increase in muscle tone, manifested by a catch and release or by minimal resistance at the end of the range of motion when the affected part(s) is moved in flexion or extension
1+	Slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the range of movement (ROM)
2	More marked increase in muscle tone through most of the ROM, but affected part(s) easily moved
3	Considerable increase in muscle tone, passive movement difficult
4	Affected part(s) rigid in flexion or extension

1.30 Reduced Upper Extremity Motor Activity Log Questionnaire

This is a structured interview that examines how much and how well subjects use their paretic arm. Subjects are instructed to rate what they were actually able to do, not what they thought they could do. Subjects are rated on the amount they use their paretic arm ("Amount Scale") and the quality of their movement during the functional activities ("How Well" Scale). The maximum score in each scale is 60, and the minimum 0.

The questionnaire includes the following 12 activities:

1. Pick up phone
2. Open a door
3. Eat finger foods
4. Control the bathroom tap
5. Pick up a glass, bottle or can
6. Brush teeth
7. Use a key to unlock the door
8. Write on a paper
9. Use the removable computer storage media (CD or floppy disk)
10. Use utensils for eating
11. Pick up a cup by the handle
12. Carry an object in the hand

Appendix 2

Newcastle and North Tyneside NHS
Health Authority

JOINT ETHICS COMMITTEE
Newcastle & North Tyneside Health Authority
University of Newcastle upon Tyne
University of Northumbria at Newcastle

Newcastle General Hospital
Westgate Road
Newcastle
NE4 6BE

Your Ref:

19 December 2001

Dr H Rodgers
Centre for Health Services Research
21 Claremont Place
NEWCASTLE UPON TYNE
NE2 4AA

Dear Dr Rodgers

Does Surface Neuromuscular Stimulation (NMES) To The Upper Limb Following Stroke Improve Outcome?
(Min Ref: 2001/320)

Your application in respect of this study was considered at the December meeting of the Joint Ethics Committee.

Before reaching a final decision in respect of your application the Committee wished:

(i) to know whether the NMES treatment will be offered to the placebo group if it is found to be effective;

(ii) to seek clarification as to why a placebo group will be included if it is likely that they will know they are not receiving the active treatment. The Committee suggested that it might be valuable to ask the patients whether they were aware which group they were in;

(iii) to seek further details regarding the method used to assess eligibility criteria such as cognitive/language impairment; and

(iv) to seek confirmation that Northumbria Healthcare NHS Trust will indemnify against any injury that results from the treatment being undertaken as well as as a result of negligence.

rodgers

Please note revised contact information

tel: (0191) 256.3295
fax: (0191) 256.3099
leonard.key@nant-ha.northy.nhs.uk

I note the information provided in your response to the Committee dated 14 December and confirm that, in the light of this information, ethical approval is granted in respect of your research study application.

Yours sincerely

Peter Heasman

Dr P A Heasman
Chairman
Joint Ethics Committee

Northumberland NHS
Health Authority

Merley Croft
Loansdean
Morpeth
Northumberland
NE61 2DL

Tel:01670 394400
Fax: 01670 394501

24 December 2001

Dr H Rodgers
Reader in Stroke Medicine
Centre for Health Services Research
21 Claremont Place
NEWCASTLE UPON TYNE
NE2 4AA

Dear Dr Rodgers

NLREC 38/2001 Does surface neuromuscular electrical stimulation (NMES) to the upper limb following acute stroke improve outcome?

Dr Church's letter confirming the remaining outstanding issue has been considered by the Chair of the LREC and I am pleased to inform you that ethical approval has now been given to your study.

Northumberland Local Research Ethics Committee is always interested in the outcome of research and would welcome a copy of any final report which may be produced. This should be sent to Dr Sue Gordon, Consultant in Public Health Medicine at the above address.

Can I also point out that in the event of any major modification in any study, the researcher is asked to resubmit the application for approval by the LREC. The Chairman of the LREC should be notified of any minor changes in the study.

Yours sincerely

MRS A YOUNG
LREC Administrator

cc Dr R Barton, R & D Dept, Northumbria Healthcare NHS Trust

2.2 Screening Questionnaire (WGH)

Does surface NMES to the upper limb following acute stroke improve outcome?

SCREENING QUESTIONNAIRE

Date of screening: Patient's name:
Ward: Patient's DOB:

1) Is the patient's usual residence in the catchment area for MCH/BCH? **NO** ❑ **YES** ❑

2) Has the patient sustained a stroke within the last 10 days? **NO** ❑ **YES** ❑

*If you have answered **NO** to question 1 and/or question 2, the patient is ineligible, therefore do not continue with this screening questionnaire.*

3) Does the patient have any other condition likely to significantly interfere with rehabilitation? **NO** ❑ **YES** ❑

4) Is the pre-stroke OHS score 4 or 5? **NO** ❑ **YES** ❑

5) Does the patient have significant UL impairment from a previous stroke affecting the same side as the current stroke? **NO** ❑ **YES** ❑

Is there an upper limb amputation or atresia (stroke-affected side)? **NO** ❑ **YES** ❑

Is there a diagnosis of frozen shoulder, dislocation or fracture of the UL (stroke-affected side) within 1 month? **NO** ❑ **YES** ❑

Is the patient taking regular analgesia specifically for the UL (stroke-affected side)? **NO** ❑ **YES** ❑

Does the patient have any of the following:
a) permanent pacemaker
b) implantable defibrillator
c) metallic shoulder implant (stroke-affected side)
d) history of life threatening cardiac arrhythmias (e.g. VF/VT)? **NO** ❑ **YES** ❑

If you have answered YES to any of questions 3 to 9, the patient is ineligible therefore please do not continue with this questionnaire.

Is the patient medically stable? **NO** ❑ **YES** ❑

6) Is the patient currently eye opening spontaneously or to speech? **NO** ❑ **YES** ❑

7) Can the patient obey the following second order commands?
a) 'Point to the ceiling and then to the curtain.'
b) 'Before pointing to the ceiling, touch the chair.' **NO** ❑ **YES** ❑

8) Does the patient have evidence of any of the following:
a) UL weakness/drift?
b) Finger nose incoordination?
c) Star cancellation fail (see over – only perform if 12a&b are 'no') **NO** ❑ **YES** ❑

*If you have answered **NO** to any of questions 10-13, the patient is ineligible. However please review questions 9 and 10 within the 10-day period following stroke as this may alter the patient's eligibility.*

Please keep ALL completed screening questionnaires in the designated file on the ward for collection by Cath Church who will visit on Tuesdays and Fridays. If the patient is eligible for the study (i.e. all the ticked boxes are in bold and capital print), please provide the patient with an information leaflet. Thank you.

2.3 Screening Questionnaire (NTGH)

Does surface NMES to the upper limb following acute stroke improve outcome?

SCREENING QUESTIONNAIRE

Date of screening: Patient's name:
Ward: Patient's DOB:

9) Is the patient's usual residence in the catchment area for MCH/BCH? **NO** ❑ **YES** ❑

10) Has the patient sustained a stroke within the last 10 days? **NO** ❑ **YES** ❑

*If you have answered **NO** to question 1 and/or question 2, the patient is ineligible, therefore do not continue with this screening questionnaire.*

11) Does the patient have any other condition likely to significantly interfere with rehabilitation? **NO** ❑ **YES** ❑

12) Is the pre-stroke OHS score 4 or 5? **NO** ❑ **YES** ❑

13) Does the patient have significant UL impairment from a previous stroke affecting the same side as the current stroke? **NO** ❑ **YES** ❑

Is there an upper limb amputation or atresia (stroke-affected side)? **NO** ❑ **YES** ❑

Is there a diagnosis of frozen shoulder, dislocation or fracture of the UL (stroke-affected side) within 1 month? **NO** ❑ **YES** ❑

Is the patient taking regular analgesia specifically for the UL (stroke-affected side)? **NO** ❑ **YES** ❑

Does the patient have any of the following:
a) permanent pacemaker
b) implantable defibrillator
c) metallic shoulder implant (stroke-affected side)
d) history of life threatening cardiac arrhythmias (e.g. VF/VT)? **NO** ❑ **YES** ❑

If you have answered YES to any of questions 3 to 9, the patient is ineligible therefore please do not continue with this questionnaire.

Is the patient medically stable? **NO** ❑ **YES** ❑

14) Is the patient currently eye opening spontaneously or to speech? **NO** ❑ **YES** ❑

15) Can the patient obey the following second order commands?
a) 'Point to the ceiling and then to the curtain.'
b) 'Before pointing to the ceiling, touch the chair.' **NO** ❑ **YES** ❑

16) Does the patient have evidence of any of the following:
a) UL weakness/drift?
b) Finger nose incoordination?
c) Star cancellation fail (see over – only perform if 12a&b are 'no') **NO** ❑ **YES** ❑

*If you have answered **NO** to any of questions 10-13, the patient is ineligible. However please review questions 9 and 10 within the 10-day period following stroke as this may alter the patient's eligibility.*

Please keep ALL completed screening questionnaires in the designated file on the ward for collection by Cath Church who will visit on Mondays and Thursdays. If the patient is eligible for the study (i.e. all the ticked boxes are in bold and capital print), please provide the patient with an information leaflet. Thank you.

2.4 Patient Information Sheet

Does surface neuromuscular electrical stimulation (NMES) to the upper limb following acute stroke improve outcome?

INFORMATION FOR PATIENTS

We would like to invite you to participate in a study about arm recovery following stroke.

Why are we doing this study?

We are constantly trying to improve the services that are available to people who have had a stroke. Arm weakness, numbness and poor co-ordination are common problems following a stroke and there is some evidence that electrical stimulation to the arm can help to improve outcome. We are conducting a study to confirm whether or not this is the case.

Do I have to agree to take part?

We hope that you will want to help us with this important study but if you choose not to take part it will not affect your care. Your participation is voluntary and you are free to withdraw at any time without giving a reason.

What is involved?

If you agree to participate in the study, we will first ask you a few questions about your stroke and examine your arm. This will take up to 20 minutes and once this assessment is completed you will be 'randomised' into one of two groups. One group will receive the electrical stimulation and the other group will receive placebo ('dummy') treatment. *Everyone in the study will still get the therapy that they would normally receive following a stroke no matter which group they are in.*

All patients in the study will need to wear the electrical stimulation equipment. The equipment is shown in the picture and is similar to a TENS machine which is used to treat pain. The electrodes that deliver the electrical current are placed on the surface of the skin around the shoulder. There are no needles involved. The basic stimulation is low (30 Hz). We are not sure whether simply wearing the electrodes is effective in improving arm recovery following a stroke or whether the electrodes need to deliver electrical current in order to be effective. It is therefore important that the 2 groups are the same in every way apart from the fact that one group receives the electrical current and the other one doesn't. This will enable us to make comparisons and to find out whether the electrical stimulation makes any difference to the function of the arm.

We are recruiting patients into the study within 10 days of their stroke. Trained staff will put the equipment on you for 30 minutes initially. Over the first week, the time you wear the equipment will gradually increase to 3 sessions (1 hour each) daily. During these sessions, you wear the equipment under your clothes and must avoid getting it wet.

The full course of electrical stimulation is four weeks but if you are to be discharged from hospital during this period, we can teach a relative, friend or carer to use the equipment so that the treatment can continue at home.

We will keep a diary to record the sessions of electrical stimulation that you receive and also to record any other treatment or therapy that you receive for your stroke.

We would like to assess your recovery at the end of the four-week treatment period and again at 3 months following your stroke. This will involve a visit to the hospital to see a member of our team who will ask you questions about your recovery and measure your arm function. If you prefer, this could be done in your own home.

Are there any side effects?

Whilst wearing the equipment, you may notice some tingling of the arm or see some mild jerking of the shoulder muscles. We have experience of using this equipment and do not expect it to cause you pain or any significant side effects.

How will this study benefit future stroke patients?

This study will involve almost 200 people who have suffered a stroke and asks an important question as to whether electrical stimulation improves the function of the arm after a stroke. As a result of this work, we shall be able to answer this question and improve care and treatment to future stroke patients.

Will information obtained from the study be confidential?

All information obtained will be entirely confidential. The data from this study may be published and will be submitted as part of a research thesis. The information however is anonymous and no individuals can be identified from the data.

Will anybody else be told about my participation in the study?
If you agree to participate, we will contact your GP to let him/her know about the study.

What if I am harmed as a result of the study?
If you are harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay for it. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanism is available to you.

What if I have further questions?

If you would like further information about this study please contact Dr. Catherine Church, The Education Centre, North Tyneside General Hospital, Rake Lane, North Shields, NE29 8NH. Telephone: 0191 293 2593 (direct line).

2.5 Screening Log

Screening No.	Date	Name	DOB	Date of admission	Ward No.	Stroke Y/N	Within 10 days Y/N	Eligible CC Y/N	Reason for exclusion

2.6 Consent Form

Does surface neuromuscular electrical stimulation (NMES) to the upper limb following acute stroke improve outcome?

CONSENT FORM

	No	Yes
Have you read the patient information sheet?	❑	❑
Have you had an opportunity to ask questions and discuss the study?	❑	❑
Have all of your questions been answered satisfactorily?	❑	❑
Have you received enough information about the study?	❑	❑

Who have you spoken to?
Dr/Mr/Ms.....

Do you understand that you are free to withdraw from the study at any time?	❑	❑
• Without having to give reason?	❑	❑
• Without affecting your future medical care?	❑	❑
• Do you agree to participate in the study?	❑	❑

If you are harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay for it. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanism is available to you.

Name (Block Capitals).....

Signature.....

Witness (Block Capitals).....

Signature.....

Date.....

2.7 Initial Assessment Form

Does surface neuromuscular electrical stimulation (NMES) to the upper limb following acute stroke improve outcome?

PERSONAL DETAILS

Date: ___/___/___ Study No. | | | |

Medical Records No. _____

Hospital _____

Ward no. _____

Patient details

Date of Birth: ___/___/___

Title: Mr Mrs Ms Miss

Name _____

Address _____

_____

Post code _____

Tel No. _____

Next of kin details

Title: Mr Mrs Ms Miss

Name _____

Address _____

_____

Post code _____

Tel No. _____

General practitioner's details

Name: _____

Address _____

_____

Post code _____

Tel No. _____

Sex: Male ☐ Female ☐

Date of stroke: __/__/__

Age: ☐☐ **Date of admission:** __/__/__

Date of randomisation __/__/__

Patient history

Is the patient right or left handed?

Right ☐ Left ☐ Ambidextrous ☐ Uncertain ☐

Has the patient had previous strokes? No ☐ Yes ☐

If no, go to Qu. 31

Side of body affected by previous strokes R ☐ L ☐ Both ☐ Uncertain ☐

Did the patient have residual neurological deficit? No ☐ Yes ☐

(Describe deficit

_____

_____)

Give the date of the last stroke _____

Other co-morbidity

Known diabetes No ☐ Yes ☐

Other relevant co-morbidity _____

New neurological impairment (from the history, medical notes and clinical examination)**

		R	L
Unilateral weakness affecting face	No ☐	Yes ☐	Yes ☐
Unilateral weakness affecting arm/hand	No ☐	Yes ☐	Yes ☐
Unilateral weakness affecting leg/ foot	No ☐	Yes ☐	Yes ☐
Sensory deficit affecting face	No ☐	Yes ☐	Yes ☐
Sensory deficit affecting arm/hand	No ☐	Yes ☐	Yes ☐
Sensory deficit affecting leg/foot	No ☐	Yes ☐	Yes ☐
Homonymous hemianopia	No ☐	Yes ☐	Yes ☐
Visuospatial disorder e.g. sensory inattention	No ☐	Yes ☐	Yes ☐
Brainstem/cerebellar signs	No ☐	Yes ☐	Yes ☐
Other deficit	No ☐	Yes ☐	Yes ☐
Dysphasia		No ☐	Yes ☐

Oxford Handicap Scale

Please tick one box only

Before your recent stroke, which one of the following best describes you:

0 I had no symptoms at all and coped well with life..... ☐

1 I had a few symptoms but these did not interfere with my everyday life..... ☐

2 I had symptoms which had caused some changes in my life but I was still able to look after myself ..... ☐

3 I had symptoms which had significantly changed my life and prevented me from coping fully, and I needed some help in looking after myself ..... ☐

4 I had quite severe symptoms which meant that I needed to have help from other people but I was not so bad as to need attention day and night ..... ☐

5 I had major symptoms which severely handicapped me and I needed constant attention day and night ..... ☐

Score ☐

Pre-stroke Pain Scale

In the month prior to your recent stroke, did you have pain in your arms for most days? No ☐ Yes ☐

If yes, which arm(s) has been painful? R ☐ L ☐ Both ☐

How would you describe this pain (mark one only)?

Excruciating (very severe)
Severe
Moderate
Mild
None

If 0 (zero) is no pain at all, and the number 10 (ten) means as painful as it could be, then how painful was it? (please give a number between one and ten)

_____

Post-stroke Pain Scale

Since your recent stroke, have you had any pain in your arms? No ☐ Yes ☐

If yes, which arm(s) has been painful? R ☐ L ☐ Both ☐

How would you describe this pain (mark one only)?

Excruciating (very severe)
Severe
Moderate
Mild
None

If 0 (zero) is no pain at all, and the number 10 (ten) means as painful as it could be, then how painful was it? (please give a number between one and ten)

_____

Nottingham Extended-ADL Index

Before your recent stroke, were you living alone? No ☐ Yes ☐ Don't know ☐

	Not at all	***With help***	***Alone with difficulty***	***Alone easily***
a) Mobility				
In the month before your stroke, did you:				
• walk around outside?	☐	☐	☐	☐
• climb stairs?	☐	☐	☐	☐
• get in and out of the car?	☐	☐	☐	☐
• walk over uneven ground?	☐	☐	☐	☐
• cross roads?	☐	☐	☐	☐
• travel on public transport?	☐	☐	☐	☐
b) In the kitchen				
In the month before your stroke, did you:				
• manage to feed yourself?	☐	☐	☐	☐
• manage to make yourself a hot drink?	☐	☐	☐	☐
• take hot drinks from one room to another?	☐	☐	☐	☐
• do the washing up?	☐	☐	☐	☐
• make yourself a hot snack?	☐	☐	☐	☐
c) Domestic tasks				
In the month before your stroke, did you:				
• manage your own money when you were out?	☐	☐	☐	☐
• wash small items of clothing?	☐	☐	☐	☐
• do your own shopping?	☐	☐	☐	☐
• do your own housework?	☐	☐	☐	☐
• do a full clothes wash?	☐	☐	☐	☐
d) Leisure Activities				
In the month before your stroke, did you:				
• read newspapers or books?	☐	☐	☐	☐
• use the telephone?	☐	☐	☐	☐
• write letters?	☐	☐	☐	☐
• go out socially?	☐	☐	☐	☐
• manage your own garden?	☐	☐	☐	☐
• drive a car?	☐	☐	☐	☐

Scoring

0= Not at all 1 = With help 2 = On my own with difficulty 3 = Alone easily

Abbreviated Mental Health Test Scores

Age	☐
Time (to nearest hour)	☐
Address: 42 West Street	☐
Name of Hospital	☐
Year	☐
Date of Birth	☐
Month	☐
Years of First World War	☐
Name of monarch	☐
Count backwards from 20 - 1	☐
Score	☐ ☐

Sheffield Aphasia Screening Test for Acquired Language Disorders

RECEPTIVE SKILLS

Score 1 for correct answer
Score 0 for incorrect answer

a. Verbal comprehension of single words

I'm going to ask you to point to some of the things in the room

Score ☐

door ☐ light ☐ chair ☐
ceiling ☐ corner ☐

b. Comprehension of sequential command

i) point to the ceiling and then to the curtain ☐

ii) before pointing to the ceiling, touch the chair ☐

c. Comprehension of a complex command

Tap the chair twice with a clenched fist, while looking at the ceiling ☐

d. Recognition of differences in meaning between words

I'm going to read you a list of words and I want you to tell me which is the odd one out:

i) chicken, duck, apple, turkey ☐

ii) run, drink, walk, sprint ☐

iii) small, large, massive, huge ☐

e. Comprehension of a narrative

i) I'm going to read you a short paragraph and then ask you a question about it.
John went to the shop to buy a pen. When he got there he found that he had forgotten his wallet, so he came home and made himself a cup of tea.

What should he have taken with him? ☐

ii) I'm going to read you another paragraph.

Mrs Smith visited several shops. She bought a newspaper, a cauliflower, a stamp and some sausages.

What was the second shop she visited ? ☐

Receptive skills total score ☐

EXPRESSIVE SKILLS

Score 1 for correct answer
Score 0 for incorrect answer

f. Word finding

Tell me the names of three well-known places in client's home town.

Score one mark if three names are given correctly 

g. Abstract word finding

Tell me another word that means the same as:

i) beautiful ; 

ii) angry; 

iii) ridiculous 

h. Sequencing

Describe how you would make a cup of tea. 

A correct answer contains two or more appropriate stages in the right order.

i. Definitions

Describe what the following words mean:

i) home; 

ii) search; 

iii) ambitious . 

j. Verbal reasoning

I'd like you to tell me:

i) why you would use an umbrella; 

ii) why people go on holiday; 

iii) what would you do if you were locked out of the house. 

Expressive skills total score 

Receptive and expressive skills total score 

Motricity Index

Arm (in sitting position)

A. Pinch grip; 2.5cm cube between thumb and forefinger
B. Elbow flexion; from 90 degrees, voluntary contraction/movement
C. Shoulder abduction; from against chest

A. Pinch grip

0	No movement
11	Beginnings of prehension (any movement of finger or thumb)
19	Grips cube, but unable to hold against gravity
22	Grips cube, held against gravity, but not against weak pull
26	Grips cube against pull, but weaker than other side
33	Normal pinch grip

Score R arm ☐☐ Score L arm ☐☐

B. Elbow flexion

0	No movement
9	Palpable contraction in muscle, but no movement
14	Movement seen, but not full range/not against gravity
19	Movement; full range against gravity, not against resistance
25	Movement against resistance, but weaker than other side
33	Normal power

Score R arm ☐☐ Score L arm ☐☐

C. Shoulder abduction

0	No movement
9	Palpable contraction in muscle, but no movement
14	Movement seen, but not full range/not against gravity
19	Movement; full range against gravity, not against resistance
25	Movement against resistance, but weaker than other side
33	Normal power

Score R arm ☐☐ Score L arm ☐☐

Leg (in sitting position)
D. Ankle dorsiflexion; from plantar flexed position
E. Knee extension; from 90 degrees, voluntary contraction/movement
F. Hip flexion; usually from 90 degrees

D. Ankle Dorsiflexion

0	No movement
9	Palpable contraction in muscle, but no movement
14	Movement seen, but not full range/not against gravity
19	Movement; full range against gravity, not against resistance
25	Movement against resistance, but weaker than other side
33	Normal power

Score R leg ☐☐ Score L leg ☐☐

E. Knee Extension

0	No movement
9	Palpable contraction in muscle, but no movement
14	Movement seen, but not full range/not against gravity
19	Movement; full range against gravity, not against resistance
25	Movement against resistance, but weaker than other side
33	Normal power

Score R leg ☐☐ Score L leg ☐☐

F. Hip Flexion

0	No movement
9	Palpable contraction in muscle, but no movement
14	Movement seen, but not full range/not against gravity
19	Movement; full range against gravity, not against resistance
25	Movement against resistance, but weaker than other side
33	Normal power

Score R leg ☐☐ Score L leg ☐☐

Arm score = scores (1) + (2) + (3) + 1 (to make 100) ***Leg scores (4) + (5) + (6) + 1 (to make 100)***

TOTAL RIGHT LEG ☐☐☐ **TOTAL LEFT LEG** ☐☐☐

TOTAL RIGHT ARM ☐☐☐ **TOTAL LEFT ARM** ☐☐☐

Side score = (ARM + LEG)/2

RIGHT SIDE ☐☐☐ **LEFT SIDE** ☐☐☐

Frenchay Arm Test

Instructions

The patient sits at a table with his/her hands on his/her lap. Each task starts from this position. The patient scores one for each task completed successfully (and nought if he/she fails), and is asked to use each hand to:

	R	L
1. Stabilise a ruler while drawing a line with a pencil held in the other hand. To pass, the ruler must be held firmly.	☐	☐
2. Grasp a cylinder (12mm diameter, 5cm long) set on its end approximately 15cm from the table edge, lift it about 30cm and replace it without dropping.	☐	☐
3. Pick up a glass half-full of water positioned 15-30cm from the table edge, drink some water and replace the glass without spilling any water.	☐	☐
4. Remove and replace a sprung clothes peg from a 10mm diameter dowel, 15cm long, set in a 10cm square base, placed 15-30cm from the table edge. He/she is not to drop the peg or knock the dowel over.	☐	☐
5. Comb his/her hair (or imitate); he/she must comb across the top, down the back and down each side of the head.	☐	☐

TOTAL SCORES:

RIGHT ☐ **LEFT** ☐

Action Research Arm Test

Instructions - There are four subtests : Grasp, Grip, Pinch and Gross movement.
If a subject passes the first the first task in each subtest then they score top marks and move onto the .next subtest. If a subject fails the first and the second task in a subtest, then they score zero overall for that subtest and move onto the next. The patient must be able to sit unaided in order to attempt the test. If not, the patient scores 0.

Score 0 = can perform no part of the test
1 = performs test partially
2 = completes test, but takes abnormally long time
3 = performs test normally.
Start with the least impaired arm first.

ARAT done
Unable to sit (score 0)
ARAT not done
(Give reason _____)

	R	L
a) Grasp		
1. 10cm cube (if score = 3 then total = 18 & go to *Grip*)		
2. 2.5cm cube (if Grasp score = 0 so far then Grasp total = 0 & go to *Grip*)		
3. 5cm cube		
4. 7.5cm cube		
5. cricket ball		
6. stone		
Grasp total		
b) Grip		
1. Pour water glass to glass (if score = 3 then total = 12 & go to *Pinch*)		
2. 2.25cm tube (if Grip score = 0 so far then Grip total = 0 & go to *Pinch*)		
3. 1cm tube		
4. washer over bolt		
Grip total :		
c) Pinch		
1. 6mm bearing 3rd finger & thumb (if score = 3 then total = 18 & go to *Gross*)		
2. marble index & thumb (if Pinch score = 0 so far then Pinch total = 0 & go to *Gross*)		
3. 6mm bearing 2nd finger & thumb		
4. 6mm bearing 1st finger & thumb		
5. marble 2nd finger & thumb		
6. marble 3rd finger & thumb		
Pinch total		
d) Gross		
1. Place hand behind head (if score = 3 then total = 9 & finish)		
2. Place hand on top of head		
3. Hand to mouth		
4.		
Gross total :		
ARAT Total		

Shoulder Shrug Test

- Subject should be sitting up straight.
- Ask subject to shrug both shoulders together.
- Observer watches for symmetry and then attempts to push down the shoulders.
- Normally it is not possible to force someone's shoulders down with moderate effort.
- Score each side in turn :

Scoring

0 = no shoulder elevation at all

1 = elevation of the shoulder, but less marked or weaker than the other side

2 = unable to force down the shoulder.

RIGHT SIDE ☐ **LEFT SIDE** ☐

National Institute of Health Stroke Scale

a) Level of consciousness
0 = Alert, keenly responsive
1 = Drowsy, but rousable by minor stimulation to obey, answer, or respond
2 = Stuporous, requires repeated stimulation to attend, or lethargic or obtunded, requiring strong or painful stimulation to make movements.
3 = Coma, responds only with reflex motor or autonomic effects, or unresponsive.

SCORE ☐

b) Level of consciousness - questions
Ask patient the month and his/her age. Score first answer.
0 = Answers both correctly
1 = Answers one correctly
2 = Incorrect

SCORE ☐

c) Level of consciousness – commands
Ask patient to open/close hand and eyes. Score if he/she makes unequivocal attempt.
0 = Obeys both correctly
1 = Obeys one correctly
2 = Incorrect

SCORE ☐

d) Pupillary response
0 = Both reactive
1 = One reactive
2 = Neither reactive

SCORE ☐

e) Best gaze
0 = Normal
1 = Partial gaze palsy; abnormal but not forced deviation
2 = Forced deviation/total gaze paresis

SCORE ☐

f) Best visual
Confrontation testing using finger movements, including double simultaneous stimulation. Use visual threat if consciousness or comprehension limit testing, scoring '1' for any asymmetry demonstrated.
0 = No visual loss
1 = Partial hemianopia
2 = Complete hemianopia, to within 5 degrees of fixation

SCORE ☐

g) Facial palsy
0 = Normal
1 = Minor
2 = Partial
3 = Complete

SCORE ☐

h) Best motor - arm
Arms held for 10 seconds at 90 degrees if sitting, 45 degrees if lying. Grade weaker arm. Place arms in position if comprehension reduced.
0 = No drift in 10 seconds
1 = Drift, after brief hold
2 = Cannot resist gravity, falling immediately but some effort made
3 = No effort against gravity

RIGHT SIDE ☐ **LEFT SIDE** ☐

i) Best motor – leg
While lying, patient to hold weaker leg raised 30 degrees for 5 sec. Place leg if comprehension reduced.
0 = No drift in 5 seconds
1 = Drift, lowering within 5 sec
2 = Cannot resist gravity, falling to bed but some effort made
3 = No effort against gravity

RIGHT SIDE ☐ **LEFT SIDE** ☐

j) Plantar reflex
0 = Normal
1 = Equivocal
2 = One extensor
3 = Bilateral extensor

SCORE ☐

k) Limb ataxia
Finger-nose and heel-shin tests performed; ataxia is only scored if out of proportion to weakness. If total paralysis, score as absent.
0 = Absent
1a = Present in arm
1b= Present in leg
2 = Present in arm and leg

RIGHT SIDE ☐ **LEFT SIDE** ☐

l) Sensory
Tested with pin; only hemisensory loss scored. If comprehension or consciousness reduced, only score if obvious evidence.
0 = Normal
1 = Partial loss, subjectively different but still felt
2 = Dense loss, unaware of being touched

RIGHT SIDE ☐ **LEFT SIDE** ☐

m) Neglect
0 = No neglect
1 = Partial neglect, visual, tactile or auditory
2 = Complete neglect, affecting more than one modality

RIGHT ☐ **LEFT** ☐

n) Dysarthria
0 = Normal articulation
1 = Mild to moderate dysarthria, slurring some words
2 = Near unintelligible or worse

SCORE ☐

o) Best language
Assessed from responses during evaluation.
0 = No aphasia
1 = Mild to moderate aphasia; naming errors, paraphrasias, etc.
2 = Severe aphasia
3 = Mute

SCORE ☐

TOTAL NIH SCORE ☐☐

Star Cancellation Test

- Place the star chart flat in front of the subject so that the central arrow of the page is in the subject's midline.
- Explain that this is a page full of small stars, big stars and letters.
- You are going to ask them to cross out all the small stars that they can see on the page.
- Demonstrate by crossing out the two small stars immediately above the arrow.
- Give the pen to the subject, or if they are unable to hold the pen ask them to point to the small stars so that you can then cross them out.
- Continue to cross out stars until the subject confirms that they cannot see any more.
- There is no time limit, but do not prompt subject or move the page once it has been put in the midline.
  Score : number of stars subject crossed out = _____ (max = 54)

PASS (52 - 54) ☐ **FAIL (0 - 51)** ☐

Measurement of humeral external rotation (goniometer)

Measure with the patient's elbow flexed and the shoulder internally rotated so that the forearm is across the chest. Place the goniometer below the arm in a horizontal position with its circle beneath the elbow. Move one prong of the goniometer with the forearm whilst passively externally rotating the patient's arm at the shoulder. Keep the other prong in its original position whilst doing this. Read off the range of movement from the goniometer in degrees. Repeat with active humeral external rotation.

Passive range of pain-free movement _____ (degrees)

Active range of pain-free movement _____ (degrees)

Basic testing of sharp-dull and hot-cold discrimination

Use 2 empty plain blood tubes. Fill one tube with hot water from the tap (this should feel hot to your own skin but not painful and will be approximately 40-50C) and the other with cold water (room temperature). Ensure that it is obvious to you which is hot and which is cold to the touch. Test the affected upper arm, forearm and hand (with the patient's eyes closed), and mark as deficit if the patient cannot tell the difference between hot and cold in any or all of the areas.

Hot-cold discrimination deficit No ☐ Yes ☐

Use a neurotip to test the affected upper arm, forearm and hand (with the patient's eyes closed), and mark as deficit if the patient cannot tell the difference between the sharp and dull ends of the neurotip in any or all of the areas.

Sharp-dull discrimination deficit No ☐ Yes ☐

Measurement of upper arm girth

On the affected arm, measure the upper arm girth with a tape measure wrapped around the upper arm from the axillary fold. Measure the distance from the acromial process to the tape to aid accuracy of repeat measurements.

Upper arm girth (in cm) _____

Distance from acromion to tape (in cm) _____

CT head scan

Not done ☐

Assumed infarct (no clinically relevant infarct on CT) ☐

Clinically relevant infarct on CT ☐

Intracerebral haemorrhage ☐

CT head scan report (if necessary)

(**Cross-check the details for 'New neurological impairment' on page 2 now that all the assessments are complete).

Stroke subtype

TACS ☐

PACS ☐

LACS ☐

POCS ☐

Uncertain ☐

2.8 GP Letter

Dear Dr

Re. 'Does surface neuromuscular electrical stimulation (NMES) to the upper limb following acute stroke improve outcome?'

Your patient has agreed to participate in the above study taking place at North Tyneside General Hospital, Wansbeck Hospital and Morpeth Cottage Hospital.

Loss of upper limb function is a common and distressing problem following stroke. Electrical stimulation with surface electrodes is a popular therapy for stroke patients with upper limb pain but further research is needed to evaluate the effect of this treatment on recovery and pain.

We are currently undertaking a randomised-controlled trial to evaluate surface NMES in acute stroke. We are randomising patients within 10 days of stroke to receive either surface NMES or placebo for a four-week intervention period.

The intervention comprises a standard programme of NMES to the upper limb. Two surface electrodes placed over supraspinatus and posterior deltoid on the stroke-affected side are used and the basic stimulation frequency is low (30 Hz). The duration of treatment is increased slowly during the 1st week until 3 x 1 hour treatment sessions per day are achieved. This is then administered daily for the next three weeks. Where possible, patients who leave hospital before the end of the four-week intervention period will continue to receive surface NMES in their own home. Training will be given to patients, carers and support workers to enable them to use the equipment.

Control subjects receive 'sham' electrical stimulation according to the same schedule as the intervention group. The 'sham' equipment identical to the surface NMES equipment, but an internal disconnection prevents any current being delivered.

We will assess outcome at the end of the intervention period and at 3 months after stroke in terms of arm function, disability and pain. Patients may notice tingling of the arm and some involuntary muscle movement during the treatment. However, as we have experience in electrical stimulation and are using a recognised protocol, we do not anticipate any significant problems.

If you would like further information, please contact Dr. Catherine Church, Teaching and Research Fellow in Stroke Medicine. Telephone 0191 293 2593 (direct line) or air pager via North Tyneside Hospital switchboard.

Yours sincerely,

Helen Rodgers

Dr. Helen Rodgers

Reader in Stroke Medicine

2.9 Information for General Practitioners

Does surface neuromuscular electrical stimulation (sNMES) to the upper limb following acute stroke improve outcome?

INFORMATION FOR GENERAL PRACTITIONERS

Your patient has agreed to participate in the above study taking place at North Tyneside General Hospital and Wansbeck Hospital.

Loss of upper limb function is a common and distressing problem following stroke. The literature is unclear about the effectiveness of upper limb rehabilitation strategies and there is need to identify interventions that will improve upper limb function and reduce the incidence of shoulder pain.

Electrical stimulation with surface electrodes is a popular therapy for stroke patients with upper limb pain but further research is needed to evaluate the effect of this treatment on recovery and pain.

We are currently undertaking a randomised-controlled trial to evaluate surface neuromuscular electrical stimulation (NMES) in acute stroke. We are randomising patients within 10 days of stroke to receive either surface NMES or placebo for a four-week intervention period.

The intervention will comprise of a standard programme of sNMES to the upper limb. Two surface electrodes placed over supraspinatus and posterior deltoid on the stroke-affected side will be used and the basic stimulation frequency will be 30 Hz. The duration of treatment will be steadily increased over the first week until 3 x 1 hour treatment sessions per day are achieved. This will then be administered daily for the next three weeks. Where possible, patients who leave hospital before the end of the four-week intervention period will continue to receive surface NMES in their own home. Training will be given to patients, carers and support workers to enable them to use the equipment.

Control subjects will receive 'sham' electrical stimulation according to the same schedule as the intervention group. The 'sham' equipment will be identical to the surface NMES equipment, but an internal disconnection will prevent any current being delivered.

We will assess outcome at the end of the intervention period and at 3 months after stroke in terms of arm function, disability and pain.

Patients may notice tingling of the arm and some involuntary muscle movement during the treatment. However, as we have experience in electrical stimulation and are using a recognised protocol, we do not anticipate any significant problems.

If you would like further information, please contact Dr. Catherine Church, Teaching and Research Fellow in Stroke Medicine, North Tyneside General Hospital, Rake Lane, North Shields, NE29 8NH. Telephone 0191 293 2593 (direct line).

2.10 Barthel ADL Index 7 days post stroke

Function	Description		Score
Bowels	Incontinent (or needs to be given enema)	0	☐
	Occasional accidence (once a week)	1	
	Continent	2	
Bladder	Incontinent, or catheterised and unable to manage	0	☐
	Occasional accident (max. once per 24 hours)	1	
	Continent (for more than 7 days)	2	
Grooming	Needs help with personal care: face, hair, teeth, shaving	0	☐
	Independent (implements provided)	1	
Toilet Use	Dependent	0	☐
	Needs some help but can do some things alone	1	
	Independent (one and off, wiping, dressing)	2	
Feeding	Unable	0	☐
	Needs help in cutting, spreading butter etc.	1	
	Independent (food provided within reach)	2	
Transfer	Unable - no sitting balance	0	☐
	Major help (physical, 1 or 2 people), can sit	1	
	Minor help (verbal or physical)	2	
	Independent	3	
Mobility	Immobile	0	☐
	Wheelchair independent, including corners etc.	1	
	Walks with help of one person (verbal or physical)	2	
	Independent	3	
Dressing	Dependent	0	☐
	Needs help but can do about half unaided	1	
	Independent (including buttons, zips, laces etc.)	2	
Stairs	Unable	0	☐
	Needs help (verbal, physical, carrying aid)	1	
	Independent up and down	2	
Bathing	Dependent	0	☐
	Independent (Bath: must get in and out unsupervised and wash self. Shower: unsupervised/unaided.	1	
Total (0-20)			☐☐

2.11 Patient Records Label

THIS PATIENT IS PARTICIPATING IN A STUDY EVALUATING THE EFFECTS OF ELECTRICAL STIMULATION TO THE UPPER LIMB AFTER STROKE.

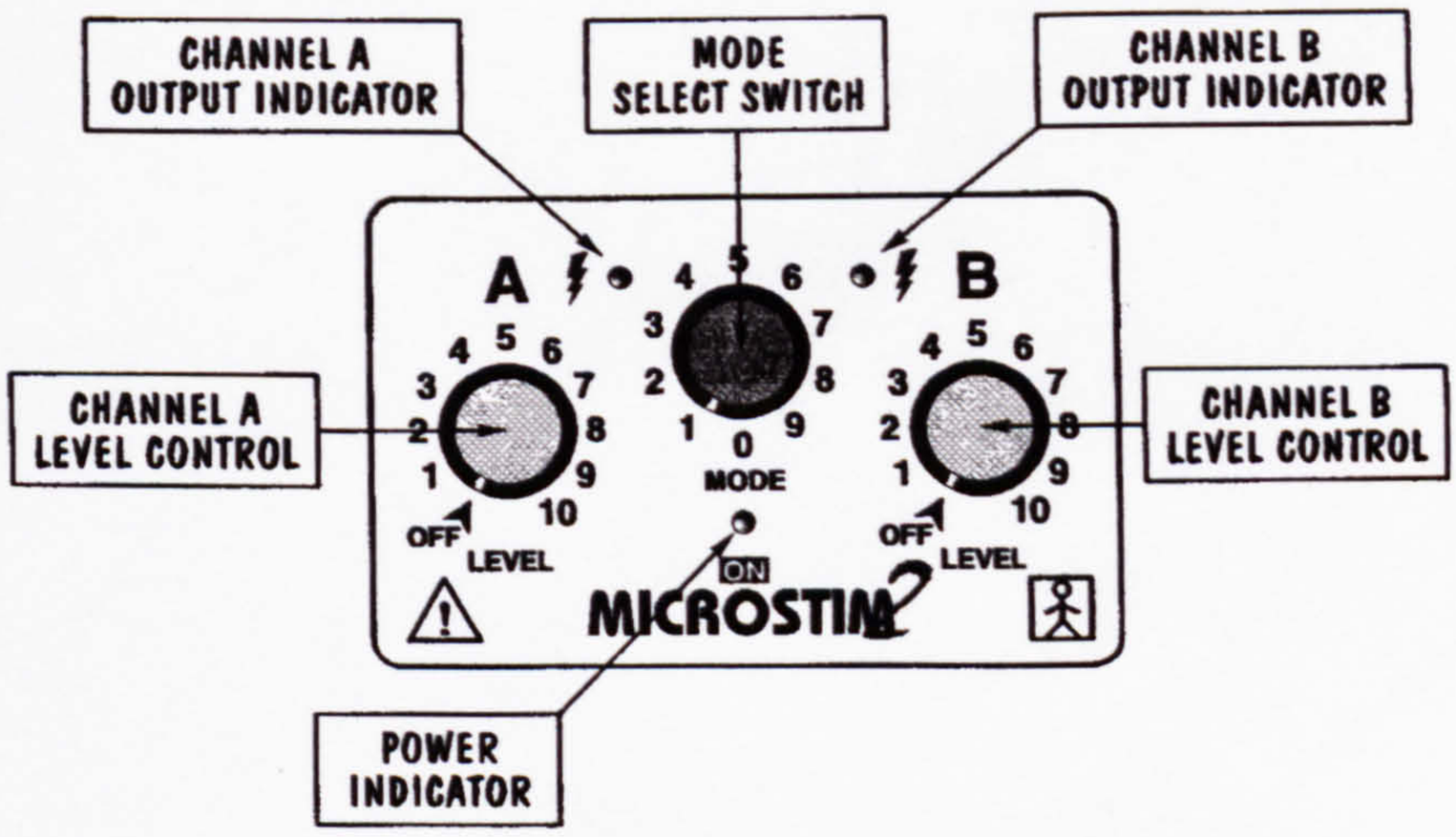
Completion Date: 31/05/2004

For further details, please contact:
Dr. Cath Church at
North Tyneside General Hospital on
0191 293 2593 (direct line).

2.12 Instruction Sheet

Does surface neuromuscular electrical stimulation (NMES) to the upper limb following acute stroke improve outcome?

INSTRUCTIONS FOR APPLYING AND USING NMES



1. Take the box, wires and electrodes out of the packet and ensure that the box number corresponds with the number written in the patient's diary.

2. **If this is the patient's first treatment session:**
   - **Write the patient's name on a blank white sticker from the study file and stick it onto their box.**
   - Open the battery compartment – if there is a green sticker present, the box is a real stimulator (the dummy stimulators do not have a sticker here).
   - Replace the battery with a new one and discard the old one.

3. Ensure that the box is switched off (knobs A & B) and that the mode (blue knob) is set at no.2 (continuous mode).

4. Place the patient's arm in the position shown in the above picture with a pillow under the arm for support.
5. The **1st electrode site** (supraspinatus) is found by locating the mid-point of the clavicle (collarbone) and then placing the electrode on the top of the muscle directly above this point. Stick an electrode pad on this site in a horizontal position.

6. The **2nd electrode site** (deltoid) is found on the outside of the arm between the tip of the shoulder and the tip of the elbow. Locate the point on this part of the arm a third of the way down from the shoulder and this is the 2nd site. *Stick an electrode pad on this site in a horizontal position.*

7. It may be helpful to mark the sites on the arm by drawing around the electrode pads with a waterproof pen.

8. Attach the red end of the wire to the 1st site (**red on top**) and the black end to the 2nd site.

9. Attach the other end of the wire into the hole on the box marked 'A'.

10. Very slowly, turn the knob labelled 'A'. This will turn on the stimulation and a beep will sound. Turn this up until muscle movement is seen at the shoulder (the patient is likely to mention some tingling just before this happens). The movement will be a 'shrug' of the shoulder. It is best to do all this very slowly to allow the patient to get used the sensation. Stop turning knob 'A' once the muscle movement occurs. If no movement is seen by intensity level 5, stop turning 'A' anyway (see below).

11. In the placebo ('dummy') group, the box is identical to those in the intervention group but an internal disconnection prevents any current being delivered. In this case, there should be no shoulder movement seen and the intensity level (knob 'A') should not be turned up to more than 5. It is important not to indicate to the patient that this is the case so that they remain unaware of the group that they are in.

12. Now turn the mode knob to number 3 (alternate mode).

13. Write down the intensity level (knob 'A') in the patient's diary, as this should remain approximately the same for each session (if not, it may be that the battery is running low and needs replacing).

14. Please record the time the treatment session starts in the patient's diary and sign for the treatment in the patient's drug kardex.

15. A timer is provided with each box to be used for each session and will be a reminder to turn off the equipment once the treatment session is complete. This timer needs to be set to time either 30 mins or 1 hour depending on the session being given.

16. The protocol for the timing of the NMES is the same in both the intervention group and the control group and is detailed in the patient's diary and on the drug kardex.

17. During treatment sessions, the equipment must not get wet.

18. At the end of the session, turn off the stimulator (knob A) and turn the mode (blue knob) back to no. 2 ready for the next session. Record the stop time in the patient's diary.

19. In between sessions, the box is unplugged from the electrodes. The electrodes can be left in place all day unless the patient is to have a bath/shower. If this is the case, the electrodes should be removed, moistened slightly with tap water, and stuck back on their original pad. They should then be put back in their plastic bag and the bag resealed to prevent evaporation of moisture from the electrode gel.

What if there are problems?

Below is a list of possible problems with likely solutions:

NOTE that faults may be difficult to detect, as some of the stimulators are 'dummys'. For this reason, a green sticker is present in the battery compartment of each real stimulator whereas there is no sticker in the dummy ones. This means that a member of staff can determine the nature of a particular stimulator should there be concerns that there may be a fault. *It is however important that the patient is not told which stimulator they have.*

- No output and no indicator lights (for real/dummys):
  - Battery incorrectly installed – reconnect battery.
  - Exhausted battery – replace battery.
  - Faulty stimulator – inform Cath Church

- No output but the indicator lights operate (real stims):
  - Broken stimulation lead – replace lead.
  - Fault with channel A – try the stimulation using channel B instead.
  - Faulty stimulator – inform Cath Church

- The stimulator's output produces the wrong movement (real stims):
  - Incorrect electrode positions – check with diagram and/or consult other staff (e.g. ward physio/doctor, Cath Church).
  - Incorrect level of stimulation – the level may be too high or too low.

- Poor electrode contact – re-apply or replace electrodes.

- <u>The movement produced is weaker than normal</u> (real stims):
  - Insufficient stimulation – increase the stimulation level.
  - Electrode condition may be poor – replace the electrodes.

- <u>The stimulation is painful:</u>
  - Incorrect electrode positions - In particular, if the patient has pain around the 2nd electrode site, try moving the electrode pad slightly higher up the arm and try the treatment again following the above guidelines.
  - Poor electrode contact – clean and re-apply electrodes.
  - Excessively high stimulation intensity – adjust the intensity level (knob A).
  - If the treatment remains painful, try again with the red and black leads the other way round so that the black is on top.
  - If none of the above measures are successful, contact Cath Church.

- <u>The stimulator bleeps for 30 seconds and then switches itself off</u> (real/dummys):
  - Low battery – replace the battery.

Precautions

- Avoid handling the electrodes while the stimulator is on. Always remember to turn OFF the stimulator before you remove the electrodes.
- <u>Do not</u> immerse the electrodes in water. Clean them using a damp cloth.
- Always wash and dry the skin carefully when the electrodes have been removed. <u>Do not</u> use skin creams near the electrode sites.
- A slight reddening of the skin under the electrode is normal. This should fade after about an hour once the electrodes are removed. If stimulation causes long-term marking of the skin, discontinue use and contact Cath Church.
- <u>Do not</u> place electrodes over broken skin or shave the area under the electrodes as this may cause skin irritation.
- Spastic tone may be affected by electrical stimulation. If you notice any adverse change in the spasticity, discontinue use and contact Cath Church.
- <u>Do not</u> use the stimulator within 3 metres of physiotherapy short wave diathermy equipment.
- The stimulator is <u>not</u> to be used by people who have implanted electronic devices (e.g. pacemakers).

2.13 Patient Diary

WEEK 1	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7
Date							
Intensity level *							
Session 1 8am	30 mins NMES Start time_____ Stop time_____ None given ☐	30 mins NMES Start time_____ Stop time_____ None given ☐	30 mins NMES Start time_____ Stop time_____ None given ☐	30 mins NMES Start time_____ Stop time_____ None given ☐	**1 hour NMES** Start time_____ Stop time_____ None given ☐	**1 hour NMES** Start time_____ Stop time_____ None given ☐	**1 hour NMES** Start time_____ Stop time_____ None given ☐
Session 2 12pm	**No NMES**	**No NMES**	30 mins NMES Start time_____ Stop time_____ None given ☐	30 mins NMES Start time_____ Stop time_____ None given ☐	**1 hour NMES** Start time_____ Stop time_____ None given ☐	**1 hour NMES** Start time_____ Stop time_____ None given ☐	**1 hour NMES** Start time_____ Stop time_____ None given ☐
Session 3 6pm	30 mins NMES Start time_____ Stop time_____ None given ☐	30 mins NMES Start time_____ Stop time_____ None given ☐	30 mins NMES Start time_____ Stop time_____ None given ☐	30 mins NMES Start time_____ Stop time_____ None given ☐	30 mins NMES Start time_____ Stop time_____ None given ☐	30 mins NMES Start time_____ Stop time_____ None given ☐	**1 hour NMES** Start time_____ Stop time_____ None given ☐
Difficulties encountered/ reasons for non-receipt of treatment							

2.14 Newsletter

Northumbria Healthcare NHS
NHS Trust

Issue 1 April 2002

NMES Study — Hospital Newsletter

Does surface neuromuscular electrical stimulation (NMES) to the upper limb following acute stroke improve outcome?

Loss of arm function is a common and distressing problem following a stroke. Electrical stimulation is a popular therapy for stroke patients with arm pain but further research is needed to evaluate the effect of this treatment on arm recovery and pain. The NMES study began in January 2002 and is taking place in Wansbeck, North Tyneside and Morpeth Hospitals. The input of ward staff is crucial to the success of this study and the purpose of sending out regular newsletters will be to keep everyone up to date on the progress of the study.

A quick reminder of the aims of the study:

- To compare the arm function and impairment of stroke patients who receive a programme of surface NMES to the arm (the intervention group) with those receiving placebo (the control group).
- To compare the prevalence of post stroke arm pain between the intervention and control group.
- To compare disability and global health status of the intervention and control group.
- To seek the experiences and views of patients about surface NMES.

Methods

All patients admitted to North Tyneside and Wansbeck Hospitals within 10 days of acute stroke are assessed to determine whether or not they are eligible for entry into the study. Written consent is taken from eligible patients and baseline assessments are performed. The patients are then 'randomised' to receive either electrical stimulation or placebo for a 4-week period. Out-come assessments are undertaken at 4 weeks and 3 months following the stroke.

NMES

The stimulation is given 3 times daily for a 4-week period. Detailed instructions for use are found in the study files on the wards and it is vital that the sessions are recorded in the patient's diary. **If patients are to be discharged within the 4-week period, please contact Cath Church who will review them on the ward prior to discharge.**

Progress

171 patients have been screened so far and 25 eligible patients entered into the study. 16 four-week assessments are complete and the three-month assessments will commence at the beginning of April.

Lunchtime meetings!

In order to update you all further on the study and, in particular, to provide further training for staff in the use of the NMES equipment, lunchtime meetings have been arranged in each of the 3 hospitals. They will take place from 1-2pm on the following dates and a sandwich lunch will be available from 12.30pm.

- **Friday 19th April** in the Lecture Theatre, Education Centre at **Wansbeck Hospital**.
- **Tuesday 23rd April** in Classrooms 5 & 6, Education Centre at **North Tyneside Hospital.**
- **Friday 26th April** in the Committee Room on Ward 2 at **Morpeth Cottage Hospital**.

If you would like to attend, please return the slip below to Cath Church at Wansbeck Hospital or North Tyneside Hospital. This will give an idea of numbers for catering purposes.

RETURN SLIP **NMES STUDY**

I shall/shall not be able to attend the lunchtime meeting on Tuesday 23rd April (Delete as applicable)

Name _____ Ward _____

Please reply to Dr. Cath Church, Teaching and Research Fellow in Stroke Medicine, Education Centre, North Tyneside General Hospital, Rake Lane, North Shields NE29 8NH

2.15 Four-week Assessment Form

Does surface neuromuscular electrical stimulation (sNMES) to the upper limb following acute stroke improve outcome?

4-WEEK PATIENT DETAILS

4-week assessment due: ___/___/___

Name of patient _____

Dead No ☐ Yes ☐

Date of death (if applicable) _____

Patient discharged No ☐ Yes ☐

Date of discharge (if applicable) ___/___/___

Ward and hospital of death/discharge _____

Patient readmitted to hospital No ☐ Yes ☐

Details of readmission _____

Current contact address _____

_____

_____

Current type of residence

Private ☐
NH ☐
RH ☐
Hospital ☐
Other ☐

Current Tel. No. _____

Other interventions for UL pain since last stroke

None ☐
Oral analgesia ☐
Steroid injection ☐
TENS ☐
Botulinum toxin ☐
Other ☐
(please describe _____

_____)

New medical problems

_____

_____

_____

_____

New UL problems

_____

_____

_____

_____

DOES SURFACE NEUROMUSCULAR ELECTRICAL STIMULATION (sNMES) TO THE UPPER LIMB FOLLOWING ACUTE STROKE IMPROVE OUTCOME?

<<<<<<<<<<<<<<>>>>>>>>>>>>>>

FOUR - WEEK REVIEW

<<<<<<<<<<<<<<>>>>>>>>>>>>>>

Patient Name: _____

Study Number: _____

Date of Assessment: _____

Have you had any pain in your arms this week?

No ☐

Yes ☐

If yes, which arm has been painful?

Left ☐ Right ☐ Both ☐

How would you describe this pain? (mark **one** only)

Excruciating (very severe) ☐

Severe ☐

Moderate ☐

Mild ☐

None ☐

If 0 (zero) is no pain at all and 10 (ten) means as painful as it could be, then how painful was it? (Please give a number between 1 and 10).

_____

Do you take regular painkillers for pain in your arm or shoulder?

No ☐

Yes ☐

Oxford Handicap Scale - 4 week

Please tick one box only

Which one of the following best describes you:

0 I have no symptoms at all and cope well with life..... ☐

1 I have a few symptoms but these do not interfere with my everyday life ☐

2 I have symptoms which have caused some changes in my life but I am still able to look after myself ☐

3 I have symptoms which have significantly changed my life and prevented me from coping fully, and I need some help in looking after myself ☐

4 I have quite severe symptoms which mean that I need to have help from other people but I am not so bad as to need attention day and night ☐

5 I have major symptoms which severely handicap me and I need constant attention day and night ☐

Score ☐

Barthel ADL Index – 4 week

Function	Description		Score
Bowels	Incontinent (or needs to be given enema)	0	☐
	Occasional accidence (once a week)	1	
	Continent	2	
Bladder	Incontinent, or catheterised and unable to manage	0	☐
	Occasional accident (max. once per 24 hours)	1	
	Continent (for more than 7 days)	2	
Grooming	Needs help with personal care: face, hair, teeth, shaving	0	☐
	Independent (implements provided)	1	
Toilet Use	Dependent	0	☐
	Needs some help but can do some things alone	1	
	Independent (one and off, wiping, dressing)	2	
Feeding	Unable	0	☐
	Needs help in cutting, spreading butter etc.	1	
	Independent (food provided within reach)	2	
Transfer	Unable - no sitting balance	0	☐
	Major help (physical, 1 or 2 people), can sit	1	
	Minor help (verbal or physical)	2	
	Independent	3	
Mobility	Immobile	0	☐
	Wheelchair independent, including corners etc.	1	
	Walks with help of one person (verbal or physical)	2	
	Independent	3	
Dressing	Dependent	0	☐
	Needs help but can do about half unaided	1	
	Independent (including buttons, zips, laces etc.)	2	
Stairs	Unable	0	☐
	Needs help (verbal, physical, carrying aid)	1	
	Independent up and down	2	
Bathing	Dependent	0	☐
	Independent (Bath: must get in and out unsupervised and wash self. Shower: unsupervised/unaided.	1	
Total (0-20)			☐☐

Star Cancellation Test – 4 week

- Place the star chart flat in front of the subject so that the central arrow of the page is in the subject's midline.
- Explain that this is a page full of small stars, big stars and letters.
- You are going to ask them to cross out all the small stars that they can see on the page.
- Demonstrate by crossing out the two small stars immediately above the arrow.
- Give the pen to the subject, or if they are unable to hold the pen ask them to point to the small stars so that you can then cross them out.
- Continue to cross out stars until the subject confirms that they cannot see any more.
- There is no time limit, but do not prompt subject or move the page once it has been put in the midline.

  Score : number of stars subject crossed out = _____ (max = 54)

PASS (52 - 54) ☐ **FAIL (0 - 51)** ☐

Motricity Index – 4 week

Arm (in sitting position)

A. Pinch grip; 2.5cm cube between thumb and forefinger
B. Elbow flexion; from 90 degrees, voluntary contraction/movement
C. Shoulder abduction; from against chest

A. Pinch grip

0	No movement
11	Beginnings of prehension (any movement of finger or thumb)
19	Grips cube, but unable to hold against gravity
22	Grips cube, held against gravity, but not against weak pull
26	Grips cube against pull, but weaker than other side
33	Normal pinch grip

Score R arm ☐☐ Score L arm ☐☐

B. Elbow flexion

0	No movement
9	Palpable contraction in muscle, but no movement
14	Movement seen, but not full range/not against gravity
19	Movement; full range against gravity, not against resistance
25	Movement against resistance, but weaker than other side
33	Normal power

Score R arm ☐☐ Score L arm ☐☐

C. Shoulder abduction

0	No movement
9	Palpable contraction in muscle, but no movement
14	Movement seen, but not full range/not against gravity
19	Movement; full range against gravity, not against resistance
25	Movement against resistance, but weaker than other side
33	Normal power

Score R arm ☐☐ Score L arm ☐☐

Leg (in sitting position)
D. Ankle dorsiflexion; from plantar flexed position
E. Knee extension; from 90 degrees, voluntary contraction/movement
F. Hip flexion; usually from 90 degrees

E. Ankle Dorsiflexion

0	No movement
9	Palpable contraction in muscle, but no movement
14	Movement seen, but not full range/not against gravity
19	Movement; full range against gravity, not against resistance
25	Movement against resistance, but weaker than other side
33	Normal power

Score R leg ☐☐ Score L leg ☐☐

E. Knee Extension

0	No movement
9	Palpable contraction in muscle, but no movement
14	Movement seen, but not full range/not against gravity
19	Movement; full range against gravity, not against resistance
25	Movement against resistance, but weaker than other side
33	Normal power

Score R leg ☐☐ Score L leg ☐☐

F. Hip Flexion

0	No movement
9	Palpable contraction in muscle, but no movement
14	Movement seen, but not full range/not against gravity
19	Movement; full range against gravity, not against resistance
25	Movement against resistance, but weaker than other side
33	Normal power

Score R leg ☐☐ Score L leg ☐☐

Arm score = scores (1) + (2) + (3) + 1 (to make 100) ***Leg scores (4) + (5) + (6) + 1 (to make 100)***

TOTAL RIGHT LEG ☐☐☐ **TOTAL LEFT LEG** ☐☐☐

TOTAL RIGHT ARM ☐☐☐ **TOTAL LEFT ARM** ☐☐☐

Side score = (ARM + LEG)/2

RIGHT SIDE ☐☐☐ **LEFT SIDE** ☐☐☐

Shoulder Shrug Test – 4 week

- Subject should be sitting up straight.
- Ask subject to shrug both shoulders together.
- Observer watches for symmetry and then attempts to push down the shoulders.
- Normally it is not possible to force someone's shoulders down with moderate effort.
- Score each side in turn :

Scoring

0 = no shoulder elevation at all

1 = elevation of the shoulder, but less marked or weaker than the other side

2 = unable to force down the shoulder.

RIGHT SIDE ☐ **LEFT SIDE** ☐

Frenchay Arm Test – 4 week

Instructions

The patient sits at a table with his/her hands on his/her lap. Each task starts from this position. The patient scores one for each task completed successfully (and nought if he/she fails), and is asked to use each hand to:

	R	L
6. Stabilise a ruler while drawing a line with a pencil held in the other hand. To pass, the ruler must be held firmly.	☐	☐
7. Grasp a cylinder (12mm diameter, 5cm long) set on its end approximately 15cm from the table edge, lift it about 30cm and replace it without dropping.	☐	☐
8. Pick up a glass half-full of water positioned 15-30cm from the table edge, drink some water and replace the glass without spilling any water.	☐	☐
9. Remove and replace a sprung clothes peg from a 10mm diameter dowel, 15cm long, set in a 10cm square base, placed 15-30cm from the table edge. He/she is not to drop the peg or knock the dowel over.	☐	☐
10. Comb his/her hair (or imitate); he/she must comb across the top, down the back and down each side of the head.	☐	☐

TOTAL SCORES:

RIGHT ☐ **LEFT** ☐

Action Research Arm Test – 4 week

Instructions - There are four subtests : Grasp, Grip, Pinch and Gross movement.
If a subject passes the first the first task in each subtest then they score top marks and move onto the .next subtest. If a subject fails the first and the second task in a subtest, then they score zero overall for that subtest and move onto the next. The patient must be able to sit unaided in order to attempt the test. If not, the patient scores 0.

Score 0 = can perform no part of the test
1 = performs test partially
2 = completes test, but takes abnormally long time
3 = performs test normally.
Start with the least impaired arm first.

ARAT done
Unable to sit (score 0)
ARAT not done
(Give reason _____)

	R	L
a) Grasp		
7. 10cm cube (if score = 3 then total = 18 & go to *Grip*)	☐	☐
8. 2.5cm cube (if Grasp score = 0 so far then Grasp total = 0 & go to *Grip*)	☐	☐
9. 5cm cube	☐	☐
10. 7.5cm cube	☐	☐
11. cricket ball	☐	☐
12. stone	☐	☐
Grasp total	☐	☐
b) Grip		
5. Pour water glass to glass (if score = 3 then total = 12 & go to *Pinch*)	☐	☐
6. 2.25cm tube (if Grip score = 0 so far then Grip total = 0 & go to *Pinch*)	☐	☐
7. 1cm tube	☐	☐
8. washer over bolt	☐	☐
Grip total :	☐	☐
c) Pinch		
7. 6mm bearing 3rd finger & thumb (if score = 3 then total = 18 & go to *Gross*)	☐	☐
8. marble index & thumb (if Pinch score = 0 so far then Pinch total = 0 & go to *Gross*)	☐	☐
9. 6mm bearing 2nd finger & thumb	☐	☐
10. 6mm bearing 1st finger & thumb	☐	☐
11. marble 2nd finger & thumb	☐	☐
12. marble 3rd finger & thumb	☐	☐
Pinch total	☐	☐
d) Gross		
5. Place hand behind head (if score = 3 then total = 9 & finish)	☐	☐
6. Place hand on top of head	☐	☐
7. Hand to mouth	☐	☐
8.		
Gross total :	☐	☐
ARAT Total	☐	☐

Measurement of humeral external rotation (goniometer)

Measure with the patient's elbow flexed and the shoulder internally rotated so that the forearm is across the chest. Place the goniometer below the arm in a horizontal position with its circle beneath the elbow. Move one prong of the goniometer with the forearm whilst passively externally rotating the patient's arm at the shoulder. Keep the other prong in its original position whilst doing this. Read off the range of movement from the goniometer in degrees. Repeat with active humeral external rotation.

Passive range of pain-free movement _____ (degrees)

Active range of pain-free movement _____ (degrees)

Measurement of upper arm girth

On the affected arm, measure the upper arm girth with a tape measure wrapped around the upper arm from the axillary fold. Measure the distance from the acromial process to the tape to aid accuracy of repeat measurements.

Upper arm girth (in cm) _____

Distance from acromion to tape (in cm) _____

2.16 Three-month Assessment Form

Does surface neuromuscular electrical stimulation (sNMES) to the upper limb following acute stroke improve outcome?

THREE-MONTH PATIENT DETAILS

3-month assessment due: ___/___/___

Name of patient _____

Dead No ☐ Yes ☐

Date of death (if applicable) _____

Patient discharged No ☐ Yes ☐

Date of discharge (if applicable) ___/___/___

Ward and hospital of death/discharge _____

Patient readmitted to hospital No ☐ Yes ☐

Details of readmission _____

Current contact address _____

_____

_____

Current type of residence

Private ☐
NH ☐
RH ☐
Hospital ☐
Other ☐

Current Tel. No. _____

Other interventions for UL pain since last stroke

None ☐
Oral analgesia ☐
Steroid injection ☐
TENS ☐
Botulinum toxin ☐
Other ☐
(please describe _____

_____)

New medical problems (since 1 month assessment)

_____

_____

_____

_____

New UL problems (since 1 month assessment)

_____

_____

_____

Still receiving physiotherapy?

yes ☐

no ☐

DOES SURFACE NEUROMUSCULAR ELECTRICAL STIMULATION (sNMES) TO THE UPPER LIMB FOLLOWING ACUTE STROKE IMPROVE OUTCOME?

<<<<<<<<<<<<<>>>>>>>>>>>>>

THREE-MONTH REVIEW

<<<<<<<<<<<<<>>>>>>>>>>>>>

Patient Name: _____

Study Number: _____

Date of Assessment: _____

Does surface neuromuscular electrical stimulation (sNMES) to the upper limb following acute stroke improve outcome?

Have you had any pain in your arms this week?

No ☐

Yes ☐

If yes, which arm has been painful?

Left ☐ Right ☐ Both ☐

How would you describe this pain? Excruciating (very severe)
(mark **one** only)

Severe ☐

Moderate ☐

Mild ☐

None ☐

If 0 (zero) is no pain at all and 10 (ten) means as painful as it could be, then how painful was it? (Please give a number between 1 and 10).

_____

Do you take regular painkillers for pain in your arm or shoulder?

No ☐

Yes ☐

Oxford Handicap Scale – 3 month

Please tick one box only

Which one of the following best describes you:

0 I have no symptoms at all and cope well with life..... ☐

1 I have a few symptoms but these do not interfere with my everyday life..... ☐

2 I have symptoms which have caused some changes in my life but I am still able to look after myself ..... ☐

3 I have symptoms which have significantly changed my life and prevented me from coping fully, and I need some help in looking after myself ..... ☐

4 I have quite severe symptoms which mean that I need to have help from other people but I am not so bad as to need attention day and night ..... ☐

5 I have major symptoms which severely handicap me and I need constant attention day and night ..... ☐

Score ☐

Barthel ADL Index 3 months post stroke

Function	Description		Score
Bowels	Incontinent (or needs to be given enema)	0	☐
	Occasional accidence (once a week)	1	
	Continent	2	
Bladder	Incontinent, or catheterised and unable to manage	0	☐
	Occasional accident (max. once per 24 hours)	1	
	Continent (for more than 7 days)	2	
Grooming	Needs help with personal care: face, hair, teeth, shaving	0	☐
	Independent (implements provided)	1	
Toilet Use	Dependent	0	☐
	Needs some help but can do some things alone	1	
	Independent (one and off, wiping, dressing)	2	
Feeding	Unable	0	☐
	Needs help in cutting, spreading butter etc.	1	
	Independent (food provided within reach)	2	
Transfer	Unable - no sitting balance	0	☐
	Major help (physical, 1 or 2 people), can sit	1	
	Minor help (verbal or physical)	2	
	Independent	3	
Mobility	Immobile	0	☐
	Wheelchair independent, including corners etc.	1	
	Walks with help of one person (verbal or physical)	2	
	Independent	3	
Dressing	Dependent	0	☐
	Needs help but can do about half unaided	1	
	Independent (including buttons, zips, laces etc.)	2	
Stairs	Unable	0	☐
	Needs help (verbal, physical, carrying aid)	1	
	Independent up and down	2	
Bathing	Dependent	0	☐
	Independent (Bath: must get in and out unsupervised and wash self. Shower: unsupervised/unaided.	1	
Total (0-20)			☐☐

Nottingham Extended-ADL Index – 3 month

Are you living alone? No ☐ Yes ☐ Don't know ☐

	Not at all	*With help*	*Alone with difficulty*	*Alone easily*
a) Mobility				
In the last month, did you:				
• walk around outside?	☐	☐	☐	☐
• climb stairs?	☐	☐	☐	☐
• get in and out of the car?	☐	☐	☐	☐
• walk over uneven ground?	☐	☐	☐	☐
• cross roads?	☐	☐	☐	☐
• travel on public transport?	☐	☐	☐	☐
b) In the kitchen				
In the last month, did you:				
• manage to feed yourself?	☐	☐	☐	☐
• manage to make yourself a hot drink?	☐	☐	☐	☐
• take hot drinks from one room to another?	☐	☐	☐	☐
• do the washing up?	☐	☐	☐	☐
• make yourself a hot snack?	☐	☐	☐	☐
c) Domestic tasks				
In the last month, did you:				
• manage your own money when you were out?	☐	☐	☐	☐
• wash small items of clothing?	☐	☐	☐	☐
• do your own shopping?	☐	☐	☐	☐
• do your own housework?	☐	☐	☐	☐
• do a full clothes wash?	☐	☐	☐	☐
d) Leisure Activities				
In the last month, did you:				
• read newspapers or books?	☐	☐	☐	☐
• use the telephone?	☐	☐	☐	☐
• write letters?	☐	☐	☐	☐
• go out socially?	☐	☐	☐	☐
• manage your own garden?	☐	☐	☐	☐
• drive a car?	☐	☐	☐	☐

Scoring

0= Not at all 1 = With help 2 = On my own with difficulty 3 = Alone easily

Star Cancellation Test – 3 month

- Place the star chart flat in front of the subject so that the central arrow of the page is in the subject's midline.
- Explain that this is a page full of small stars, big stars and letters.
- You are going to ask them to cross out all the small stars that they can see on the page.
- Demonstrate by crossing out the two small stars immediately above the arrow.
- Give the pen to the subject, or if they are unable to hold the pen ask them to point to the small stars so that you can then cross them out.
- Continue to cross out stars until the subject confirms that they cannot see any more.
- There is no time limit, but do not prompt subject or move the page once it has been put in the midline.

  Score : number of stars subject crossed out = _____ (max = 54)

PASS (52 - 54) ☐ **FAIL (0 - 51)** ☐

Motricity Index – 3 month

Arm (in sitting position)

A. Pinch grip; 2.5cm cube between thumb and forefinger
B. Elbow flexion; from 90 degrees, voluntary contraction/movement
C. Shoulder abduction; from against chest

A. Pinch grip

0	No movement
11	Beginnings of prehension (any movement of finger or thumb)
19	Grips cube, but unable to hold against gravity
22	Grips cube, held against gravity, but not against weak pull
26	Grips cube against pull, but weaker than other side
33	Normal pinch grip

Score R arm ☐☐ Score L arm ☐☐

B. Elbow flexion

0	No movement
9	Palpable contraction in muscle, but no movement
14	Movement seen, but not full range/not against gravity
19	Movement; full range against gravity, not against resistance
25	Movement against resistance, but weaker than other side
33	Normal power

Score R arm ☐☐ Score L arm ☐☐

C. Shoulder abduction

0	No movement
9	Palpable contraction in muscle, but no movement
14	Movement seen, but not full range/not against gravity
19	Movement; full range against gravity, not against resistance
25	Movement against resistance, but weaker than other side
33	Normal power

Score R arm ☐☐ Score L arm ☐☐

Leg (in sitting position)

D. Ankle dorsiflexion; from plantar flexed position
E. Knee extension; from 90 degrees, voluntary contraction/movement
F. Hip flexion; usually from 90 degrees

F. Ankle Dorsiflexion

0	No movement
9	Palpable contraction in muscle, but no movement
14	Movement seen, but not full range/not against gravity
19	Movement; full range against gravity, not against resistance
25	Movement against resistance, but weaker than other side
33	Normal power

Score R leg ☐☐ Score L leg ☐☐

E. Knee Extension

0	No movement
9	Palpable contraction in muscle, but no movement
14	Movement seen, but not full range/not against gravity
19	Movement; full range against gravity, not against resistance
25	Movement against resistance, but weaker than other side
33	Normal power

Score R leg ☐☐ Score L leg ☐☐

F. Hip Flexion

0	No movement
9	Palpable contraction in muscle, but no movement
14	Movement seen, but not full range/not against gravity
19	Movement; full range against gravity, not against resistance
25	Movement against resistance, but weaker than other side
33	Normal power

Score R leg ☐☐ Score L leg ☐☐

Arm score = scores (1) + (2) + (3) + 1 (to make 100) ***Leg scores (4) + (5) + (6) + 1 (to make 100)***

TOTAL RIGHT LEG ☐☐☐ **TOTAL LEFT LEG** ☐☐☐

TOTAL RIGHT ARM ☐☐☐ **TOTAL LEFT ARM** ☐☐☐

Side score = (ARM + LEG)/2

RIGHT SIDE ☐☐☐ **LEFT SIDE** ☐☐☐

Shoulder Shrug Test – 3 month

- Subject should be sitting up straight.
- Ask subject to shrug both shoulders together.
- Observer watches for symmetry and then attempts to push down the shoulders.
- Normally it is not possible to force someone's shoulders down with moderate effort.
- Score each side in turn :

Scoring

0 = no shoulder elevation at all

1 = elevation of the shoulder, but less marked or weaker than the other side

2 = unable to force down the shoulder.

RIGHT SIDE ☐ **LEFT SIDE** ☐

Frenchay Arm Test – 3 month

Instructions

The patient sits at a table with his/her hands on his/her lap. Each task starts from this position. The patient scores one for each task completed successfully (and nought if he/she fails), and is asked to use each hand to:

	R	L
11. Stabilise a ruler while drawing a line with a pencil held in the other hand. To pass, the ruler must be held firmly.	☐	☐
12. Grasp a cylinder (12mm diameter, 5cm long) set on its end approximately 15cm from the table edge, lift it about 30cm and replace it without dropping.	☐	☐
13. Pick up a glass half-full of water positioned 15-30cm from the table edge, drink some water and replace the glass without spilling any water.	☐	☐
14. Remove and replace a sprung clothes peg from a 10mm diameter dowel, 15cm long, set in a 10cm square base, placed 15-30cm from the table edge. He/she is not to drop the peg or knock the dowel over.	☐	☐
15. Comb his/her hair (or imitate); he/she must comb across the top, down the back and down each side of the head.	☐	☐

TOTAL SCORES:

RIGHT ☐ **LEFT** ☐

Action Research Arm Test – 3 month

Instructions - There are four subtests : Grasp, Grip, Pinch and Gross movement.
If a subject passes the first the first task in each subtest then they score top marks and move onto the .next subtest. If a subject fails the first and the second task in a subtest, then they score zero overall for that subtest and move onto the next. The patient must be able to sit unaided in order to attempt the test. If not, the patient scores 0.

Score 0 = can perform no part of the test
1 = performs test partially
2 = completes test, but takes abnormally long time
3 = performs test normally.

ARAT done
Unable to sit (score 0)
ARAT not done

(Give reason _____)

Start with the least impaired arm first.

	R	L
a) Grasp		
13. 10cm cube (if score = 3 then total = 18 & go to *Grip*)	☐	☐
14. 2.5cm cube (if Grasp score = 0 so far then Grasp total = 0 & go to *Grip*)	☐	☐
15. 5cm cube	☐	☐
16. 7.5cm cube	☐	☐
17. cricket ball	☐	☐
18. stone	☐	☐
Grasp total	☐	☐
b) Grip		
9. Pour water glass to glass (if score = 3 then total = 12 & go to *Pinch*)	☐	☐
10. 2.25cm tube (if Grip score = 0 so far then Grip total = 0 & go to *Pinch*)	☐	☐
11. 1cm tube	☐	☐
12. washer over bolt	☐	☐
Grip total :	☐	☐
c) Pinch		
13. 6mm bearing 3rd finger & thumb (if score = 3 then total = 18 & go to *Gross*)	☐	☐
14. marble index & thumb (if Pinch score = 0 so far then Pinch total = 0 & go to *Gross*)	☐	☐
15. 6mm bearing 2nd finger & thumb	☐	☐
16. 6mm bearing 1st finger & thumb	☐	☐
17. marble 2nd finger & thumb	☐	☐
18. marble 3rd finger & thumb	☐	☐
Pinch total	☐	☐
d) Gross		
9. Place hand behind head (if score = 3 then total = 9 & finish)	☐	☐
10. Place hand on top of head	☐	☐
11. Hand to mouth	☐	☐
12.		
Gross total :	☐	☐
ARAT Total	☐	☐

Measurement of humeral external rotation (goniometer)

Measure with the patient's elbow flexed and the shoulder internally rotated so that the forearm is across the chest. Place the goniometer below the arm in a horizontal position with its circle beneath the elbow. Move one prong of the goniometer with the forearm whilst passively externally rotating the patient's arm at the shoulder. Keep the other prong in its original position whilst doing this. Read off the range of movement from the goniometer in degrees. Repeat with active humeral external rotation.

Passive range of pain-free movement _____ (degrees)

Active range of pain-free movement _____ (degrees)

Measurement of upper arm girth

On the affected arm, measure the upper arm girth with a tape measure wrapped around the upper arm from the axillary fold. Measure the distance from the acromial process to the tape to aid accuracy of repeat measurements.

Upper arm girth (in cm) _____

Distance from acromion to tape (in cm) _____

Patient views about sNMES

Which stimulator were you given? Real ☐ Dummy ☐ Uncertain ☐

Did you have symptoms from the stim (e.g. tingling) No ☐ Yes ☐

Was the stim painful? No ☐ Yes ☐

How did you find the stim? _____

_____

Please review the Nottingham Health Profile questionnaire (see Appendix 1.20) with participant to ensure that all questions completed.

Questionnaire completed No ☐ Yes ☐

If no, please give reason _____

2.17 Gantt Chart

Month	Research Activity	Teaching Activity	Other
Nov-Dec 2001	Discussions with clinicians about study. Register for MD. Obtain ethical and trust approval for study. Apply for funding. Establish study – develop protocols. Test sNMES equipment and train ward staff.	Teaching sessions on the Clinical Skills course.	
Nov 2001 – Sept 2004	Monthly project meetings.	Final year teaching, dental student teaching, stage visits, accelerated visits (throughout the year).	Weekly clinic and 1 in 14 on call. SpR training days. BGS meetings bi-monthly (London).
Jan 2002 – Feb 2004	Recruit 186 patients.		
Jan 2002	Critical appraisal course.		
Feb 2002 – May 2004	4 week and 2 month follow ups		BASP/BSRG
March – May 2002	Statistics course	Hospital Clinical Practice Course – preparation, teaching and OSCE	Spring BGS Meeting (April)
June 2002		Final OSLER and OSCE. Team marking.	RITA
July 2002	Write methods section of thesis. MD assessment 1 due. 1st appraisal.	Dental OSCE examiner.	
August 2002			2 weeks in the USA
Sept – Nov 2002		Clinical Skills course – preparation, teaching and OSCE. Cert Med Ed. Away days (Oct/Nov)	Autumn BGS meeting (Oct)
Dec 2002	Poster presentation at Trust R&D day.	Stage 4 OSCE Team marking.	
Jan 2003	Poster presentation at BSRG		BASP/BSRG
Feb – Apr 2003	Critical appraisal of relevant papers for thesis introduction. Plan outline of thesis chapters. Revise methods section. 2nd appraisal. Posters for BGS and ESC.	FOCP preparation. Hospital Clinical Practice course – preparation, teaching & OSCE	Trust away days. Access course (March). Spring BGS (April).
May – June 2003	MD assessment 1 (submit report 1 month prior to this)	Write and submit portfolio for Cert Med Ed	ESC (May)
June 2003		Final OSLER and OSCE. Team marking.	RITA
June-Sept 2003		Further preparation for FOCP	
Sept – Dec 2003		FOCP course – preparation, teaching and OSCE	Autumn BGS (Oct)
Nov 2003	Submit MD assessment 3		
Dec 2003	Design results tables for thesis. Write plan/read papers for review. Plan/read for Stroke prevention paper.	FOCP teaching. Stage 4 OSCE. FOCP OSCE. Team marking. Accelerated visit.	
Jan-June 2004	Work on review and Stroke prevention paper.	Teaching on the CIDR and ID courses (fortnightly)	
Jan 2004	Submit MD assessment 3. Complete recruitment.	Stage visit	BASP/BSRG
Feb 2004	MD assessment 3		
March 2004	Complete 4 week assessments		
March-May 2004	Finalise thesis introduction		
May 2004	Complete 3 month assessments		Spring BGS
June 2004		Final OSCE and OSLER. Team marking	RITA
May-Dec 2004 (Extended until June 05 due to sick leave)	Analysis and writing of results and complete thesis. Submission of paper to peer reviewed journal.		

Does surface neuromuscular electrical stimulation (sNMES) to the upper limb following acute stroke improve outcome?

INTER-OBSERVER FORM

Motricity Index – Inter-observer

Arm (in sitting position)

A. Pinch grip; 2.5cm cube between thumb and forefinger
B. Elbow flexion; from 90 degrees, voluntary contraction/movement
C. Shoulder abduction; from against chest

A. Pinch grip

0	No movement
11	Beginnings of prehension (any movement of finger or thumb)
19	Grips cube, but unable to hold against gravity
22	Grips cube, held against gravity, but not against weak pull
26	Grips cube against pull, but weaker than other side
33	Normal pinch grip

Score R arm ☐☐ Score L arm ☐☐

B. Elbow flexion

0	No movement
9	Palpable contraction in muscle, but no movement
14	Movement seen, but not full range/not against gravity
19	Movement; full range against gravity, not against resistance
25	Movement against resistance, but weaker than other side
33	Normal power

Score R arm ☐☐ Score L arm ☐☐

C. Shoulder abduction

0	No movement
9	Palpable contraction in muscle, but no movement
14	Movement seen, but not full range/not against gravity
19	Movement; full range against gravity, not against resistance
25	Movement against resistance, but weaker than other side
33	Normal power

Score R arm ☐☐ Score L arm ☐☐

Leg (in sitting position)

D. Ankle dorsiflexion; from plantar flexed position
E. Knee extension; from 90 degrees, voluntary contraction/movement
F. Hip flexion; usually from 90 degrees

G. Ankle Dorsiflexion

0	No movement
9	Palpable contraction in muscle, but no movement
14	Movement seen, but not full range/not against gravity
19	Movement; full range against gravity, not against resistance
25	Movement against resistance, but weaker than other side
33	Normal power

Score R leg ☐☐ Score L leg ☐☐

E. Knee Extension

0	No movement
9	Palpable contraction in muscle, but no movement
14	Movement seen, but not full range/not against gravity
19	Movement; full range against gravity, not against resistance
25	Movement against resistance, but weaker than other side
33	Normal power

Score R leg ☐☐ Score L leg ☐☐

F. Hip Flexion

0	No movement
9	Palpable contraction in muscle, but no movement
14	Movement seen, but not full range/not against gravity
19	Movement; full range against gravity, not against resistance
25	Movement against resistance, but weaker than other side
33	Normal power

Score R leg ☐☐ Score L leg ☐☐

Arm score = scores (1) + (2) + (3) + 1 (to make 100) ***Leg scores (4) + (5) + (6) + 1 (to make 100)***

TOTAL RIGHT LEG ☐☐☐ **TOTAL LEFT LEG** ☐☐☐

TOTAL RIGHT ARM ☐☐☐ **TOTAL LEFT ARM** ☐☐☐

Side score = (ARM + LEG)/2

RIGHT SIDE ☐☐☐ **LEFT SIDE** ☐☐☐

Shoulder Shrug Test – Inter-observer

- Subject should be sitting up straight.
- Ask subject to shrug both shoulders together.
- Observer watches for symmetry and then attempts to push down the shoulders.
- Normally it is not possible to force someone's shoulders down with moderate effort.
- Score each side in turn :

Scoring

0 = no shoulder elevation at all

1 = elevation of the shoulder, but less marked or weaker than the other side

2 = unable to force down the shoulder.

RIGHT SIDE ☐ **LEFT SIDE** ☐

Frenchay Arm Test – Inter-observer

Instructions

The patient sits at a table with his/her hands on his/her lap. Each task starts from this position. The patient scores one for each task completed successfully (and nought if he/she fails), and is asked to use each hand to:

	R	L
16. Stabilise a ruler while drawing a line with a pencil held in the other hand. To pass, the ruler must be held firmly.	☐	☐
17. Grasp a cylinder (12mm diameter, 5cm long) set on its end approximately 15cm from the table edge, lift it about 30cm and replace it without dropping.	☐	☐
18. Pick up a glass half-full of water positioned 15-30cm from the table edge, drink some water and replace the glass without spilling any water.	☐	☐
19. Remove and replace a sprung clothes peg from a 10mm diameter dowel, 15cm long, set in a 10cm square base, placed 15-30cm from the table edge. He/she is not to drop the peg or knock the dowel over.	☐	☐
20. Comb his/her hair (or imitate); he/she must comb across the top, down the back and down each side of the head.	☐	☐

TOTAL SCORES:

RIGHT ☐ **LEFT** ☐

Action Research Arm Test – Inter-observer

Instructions - There are four subtests : Grasp, Grip, Pinch and Gross movement.
If a subject passes the first the first task in each subtest then they score top marks and move onto the .next subtest. If a subject fails the first and the second task in a subtest, then they score zero overall for that subtest and move onto the next. The patient must be able to sit unaided in order to attempt the test. If not, the patient scores 0.

Score 0 = can perform no part of the test
1 = performs test partially
2 = completes test, but takes abnormally long time
3 = performs test normally.

ARAT done
Unable to sit (score 0)
ARAT not done

(Give reason _____)

Start with the least impaired arm first.

	R	L
a) Grasp		
19. 10cm cube (if score = 3 then total = 18 & go to *Grip*)	☐	☐
20. 2.5cm cube (if Grasp score = 0 so far then Grasp total = 0 & go to *Grip*)	☐	☐
21. 5cm cube	☐	☐
22. 7.5cm cube	☐	☐
23. cricket ball	☐	☐
24. stone	☐	☐
Grasp total	☐	☐
b) Grip		
13. Pour water glass to glass (if score = 3 then total = 12 & go to *Pinch*)	☐	☐
14. 2.25cm tube (if Grip score = 0 so far then Grip total = 0 & go to *Pinch*)	☐	☐
15. 1cm tube	☐	☐
16. washer over bolt	☐	☐
Grip total :	☐	☐
c) Pinch		
19. 6mm bearing 3rd finger & thumb (if score = 3 then total = 18 & go to *Gross*)	☐	☐
20. marble index & thumb (if Pinch score = 0 so far then Pinch total = 0 & go to *Gross*)	☐	☐
21. 6mm bearing 2nd finger & thumb	☐	☐
22. 6mm bearing 1st finger & thumb	☐	☐
23. marble 2nd finger & thumb	☐	☐
24. marble 3rd finger & thumb	☐	☐
Pinch total	☐	☐
d) Gross		
13. Place hand behind head (if score = 3 then total = 9 & finish)	☐	☐
14. Place hand on top of head	☐	☐
15. Hand to mouth	☐	☐
16.		
Gross total :	☐	☐
ARAT Total	☐	☐

Inter-observer

Measurement of humeral external rotation (goniometer)

Measure with the patient's elbow flexed and the shoulder internally rotated so that the forearm is across the chest. Place the goniometer below the arm in a horizontal position with its circle beneath the elbow. Move one prong of the goniometer with the forearm whilst passively externally rotating the patient's arm at the shoulder. Keep the other prong in its original position whilst doing this. Read off the range of movement from the goniometer in degrees. Repeat with active humeral external rotation.

Passive range of pain-free movement _____ (degrees)

Active range of pain-free movement _____ (degrees)

Measurement of upper arm girth

On the affected arm, measure the upper arm girth with a tape measure wrapped around the upper arm from the axillary fold. Measure the distance from the acromial process to the tape to aid accuracy of repeat measurements.

Upper arm girth (in cm) _____

Distance from acromion to tape (in cm) _____

Appendix 3

3.1 Search Strategy for RCTs and Reviews of ES

Medline (Ovid) 1966-2004, CINAHL (Ovid) 1982-2004, Embase (Ovid) 1980-2004, and the Cochrane Controlled Trials Register.

The following terms were searched:

1. electric stimulation/
2. electric$ stimulation.tw
3. 1 or 2
4. cerebrovasc$.tw
5. stroke.tw
6. hemiplegia/
7. (hemipleg$ or hemipar$).tw
8. 4 or 5 or 6 or 7
9. upper limb
10. arm
11. shoulder
12. (upper limb$ or arm$ or shoulder$).tw
13. 9 or 10 or 11 or 12
14. 3 and 8 and 13

132 articles found on Medline (Ovid) 1966-2004; 77 found on CINAHL (Ovid) 1982-2004; 124 found on Embase (Ovid) 1980-2004; and 40 found on the Cochrane Controlled Trials Register.

RCTs and review articles (in English) of upper limb ES in stroke patients were selected.

Initially 12 RCTs and 8 review articles were assessed in detail. Other relevant articles were identified by a manual search following this.

Methodological quality of articles was assessed using the SIGN guidelines[168] (Appendix 3.2).

3.2 SIGN guidelines: Methodology Checklist for RCTs[168]

SIGN 50: A guideline developers' handbook
Notes on the use of Methodology Checklist 2: Randomised Controlled Trials

Section 1 identifies the study, the reviewer, the guideline for which the paper is being considered as evidence, and the key question(s) it is expected to address. The reviewer is asked to consider a series of aspects of RCT design and to make a judgement as to how well the current study meets this criterion. Each relates to an aspect of methodology that research has shown makes a significant difference to the conclusions of a study.

For each question in this section you should use one of the following to indicate how well it has been addressed in the study:

- Well covered
- Adequately addressed
- Poorly addressed
- Not addressed *(i.e. not mentioned, or indicates that this aspect of study design was ignored)*
- Not reported *(i.e. mentioned, but insufficient detail to allow assessment to be made)*
- Not applicable.

1.1 *The study addresses an appropriate and clearly focused question*

Unless a clear and well defined question is specified, it will be difficult to assess how well the study has met its objectives or how relevant it is to the question you are trying to answer on the basis of its conclusions.

1.2 *The assignment of subjects to treatment groups randomised*

Random allocation of patients to receive one or other of the treatments under investigation, or to receive either treatment or placebo, is fundamental to this type of study. **If there is no indication of randomisation, the study should be rejected.** If the description of randomisation is poor, the study should be given a lower quality rating. Processes such as alternate allocation, allocation by date of birth, or day of the week attending a clinic are not true randomisation processes and it is easy for a researcher to work out which patients received which treatment. These studies should therefore be classed as Controlled Clinical Trials rather than RCTs.

1.3 *An adequate concealment method is used*

Allocation concealment refers to the process used to ensure that researchers are unaware which group patients are being allocated to at the time they enter the study. Research has shown that where allocation concealment is inadequate, investigators can overestimate the effect of interventions by up to 40%. Centralised allocation, computerised allocation systems, or the use of coded identical containers would all be regarded as adequate methods of concealment, and may be taken as indicators of a well conducted study. If the method of concealment used is regarded as poor, or relatively easy to subvert, the study must be given a lower quality rating, and can be rejected if the concealment method is seen as inadequate.

1.4 *Subjects and investigators are kept 'blind' to treatment allocation*

Blinding refers to the process whereby people are kept unaware of which treatment an individual patient has been receiving when they are assessing the outcome for that patient. It can be carried out up to three levels. Single blinding is where patients are unaware of which treatment they are receiving. In double blind studies neither the doctor nor the patient knows which treatment is being given. In very rare cases studies may be triple blinded, where neither patients, doctors, nor those conducting the analysis are aware of which patients received which treatment. The higher the level of blinding, the lower the risk of bias in the study.

1.5 *The treatment and control groups were similar at the start of the trial*

Patients selected for inclusion in a trial must be as similar as possible. The study should report any significant differences in the composition of the study groups in relation to gender mix, age, stage of disease (if appropriate), social background, ethnic origin, or comorbid conditions. These factors may be covered by inclusion and exclusion criteria, rather than being reported directly. Failure to address this question, or the use of inappropriate groups, should lead to the study being downgraded.

1.6 *The only difference between the groups is the treatment under investigation*

If some patients received additional treatment, even if of a minor nature or consisting of advice and counselling rather than a physical intervention, this treatment is a potential confounding factor that may invalidate the results. **If groups were *not* treated equally, the study should be rejected unless no other evidence is available.** If the study is used as evidence it should be treated with caution.

1.7 *All relevant outcomes measured in a standard, valid and reliable way*

The primary outcome measures used should be clearly stated in the study. **If the outcome measures are not stated, or the study bases its main conclusions on secondary outcomes, the study should be rejected.** Where outcome measures require any degree of subjectivity, some evidence should be provided that the measures used are reliable and have been validated prior to their use in the study.

1.8 *What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?*

The number of patients that drop out of a study should give concern if the number is very high. Conventionally, a 20% drop out rate is regarded as acceptable, but this may vary. Some regard should be paid to why patients dropped out, as well as how many. It should be noted that the drop out rate may be expected to be higher in studies conducted over a long period of time. A higher drop out rate will normally lead to downgrading, rather than rejection of a study.

1.9 *All the subjects are analysed in the groups to which they were randomly allocate (intention to treat analysis)*

In practice, it is rarely the case that all patients allocated to the intervention group receive the intervention throughout the trial, or that all those in the comparison group do not. Patients may refuse treatment, or contra-indications arise that lead them to be switched to the other group. If the comparability of groups through randomisation is to

be maintained, however, patient outcomes must be analysed according to the group to which they were originally allocated irrespective of the treatment they actually received. (This is known as intention to treat analysis.) If it is clear that analysis was not on an intention to treat basis, the study may be rejected. If there is little other evidence available, the study may be included but should be evaluated as if it were a non-randomised cohort study.

1.10 *Where the study is carried out at more than one site, results are comparable for all sites*

In multi-site studies, confidence in the results should be increased if it can be shown that similar results were obtained at the different participating centres.

Section 2 relates to the overall assessment of the paper. It starts by rating the methodological quality of the study, based on your responses in Section 1 and using the following coding system:

++	**All or most** of the criteria have been fulfilled. Where they have not been fulfilled the conclusions of the study or review are thought very unlikely to alter.
+	**Some** of the criteria have been fulfilled. Those criteria that have not been fulfilled or not adequately described are thought unlikely to alter the conclusions.
-	**Few or no** criteria fulfilled. The conclusions of the study are thought likely or very likely to alter.

The code allocated here, coupled with the study type, will decide the **level of evidence** that this study provides.
The aim of the other questions in this section is to summarise your view of the quality of this study and its applicability to the patient group targeted by the guideline you are working on.

Section 3 asks you to summarise key points about the study that will be added to an evidence table at the next stage of the process. **It is important that you complete this section as fully as possible, and include actual data from the study wherever relevant.**

[Annex C] [Checklist]

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Scottish Intercollegiate Guidelines Network
28 Thistle Street, Edinburgh EH2 1EN
Website address: http://www.sign.ac.uk

Tel. 0131-718 5090
Fax 0131-718 5114

Web contact: duncan service@nhs net
Last modified 30/3/04

SIGN	**Methodology Checklist 2: Randomised Controlled Trials**

Study identification (*Include author, title, year of publication, journal title, pages*)

Guideline topic:	Key Question No:

Checklist completed by:

SECTION 1: INTERNAL VALIDITY

	In a well conducted RCT study.....	***In this study this criterion is::***	
1.1	The study addresses an appropriate and clearly focused question.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.2	The assignment of subjects to treatment groups is randomised	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.3	An adequate concealment method is used	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.4	Subjects and investigators are kept 'blind' about treatment allocation	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.5	The treatment and control groups are similar at the start of the trial	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.6	The only difference between groups is the treatment under investigation	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.7	All relevant outcomes are measured in a standard, valid and reliable way	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.8	What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?		
1.9	All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis)	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.10	Where the study is carried out at more than one site, results are comparable for all sites	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable

SECTION 2: OVERALL ASSESSMENT OF THE STUDY

2.1	How well was the study done to minimise bias? *Code ++, +, or –*	
2.2	If coded as +, or – what is the likely direction in which bias might affect the study results?	

2.3	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention?	
2.4	Are the results of this study directly applicable to the patient group targeted by this guideline?	
SECTION 3: DESCRIPTION OF THE STUDY (The following information is required to complete evidence tables facilitating cross-study comparisons. Please complete all sections for which information is available). *PLEASE PRINT CLEARLY*		
3.1	How many patients are included in this study? *Please indicate number in each arm of the study, at the time the study began.*	
3.2	What are the main characteristics of the patient population? *Include all relevant characteristics – e.g. age, sex, ethnic origin, comorbidity, disease status, community/hospital based*	
3.3	What intervention (treatment, procedure) is being investigated in this study? *List all interventions covered by the study.*	
3.4	What comparisons are made in the study? *Are comparisons made between treatments, or between treatment and placebo / no treatment?*	
3.5	How long are patients followed-up in the study? *Length of time patients are followed from beginning participation in the study. Note specified end points used to decide end of follow-up (e.g. death, complete cure). Note if follow-up period is shorter than originally planned.*	
3.6	What outcome measure(s) are used in the study? *List all outcomes that are used to assess effectiveness of the interventions used.*	
3.7	What size of effect is identified in the study? *List all measures of effect in the units used in the study – e.g. absolute or relative risk, NNT, etc. Include p values and any confidence intervals that are provided.*	
3.8	How was this study funded? *List all sources of funding quoted in the article, whether Government, voluntary sector, or industry.*	
3.9	Does this study help to answer your key question? *Summarise the main conclusions of the study and indicate how it relates to the key question.*	